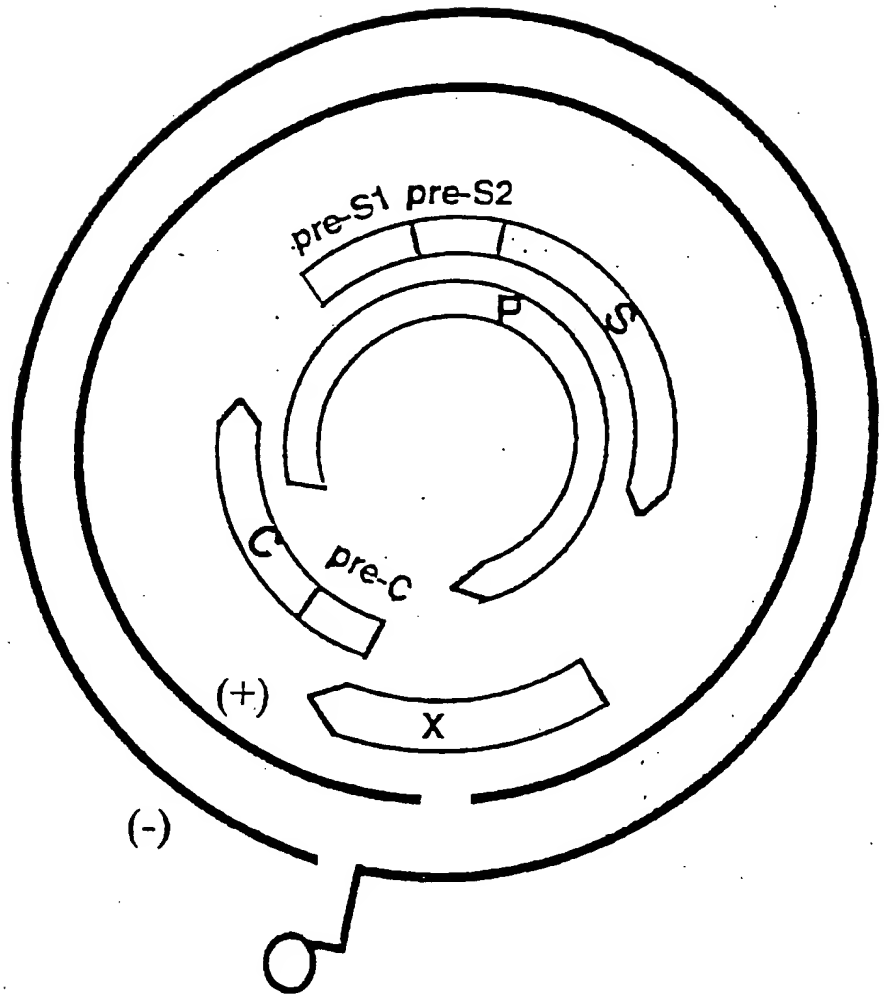
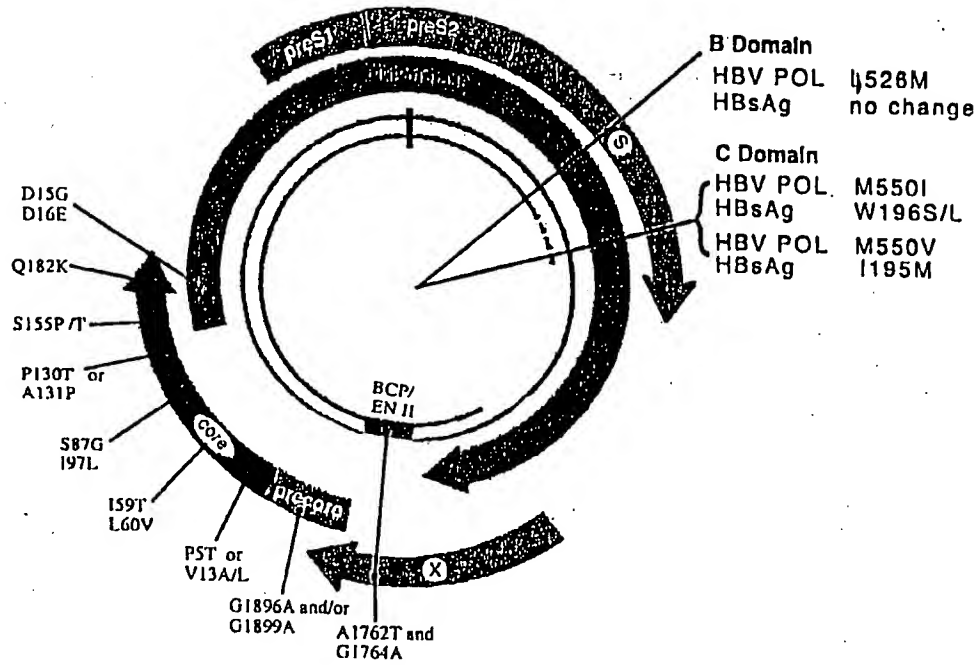


Figure 1A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preS2
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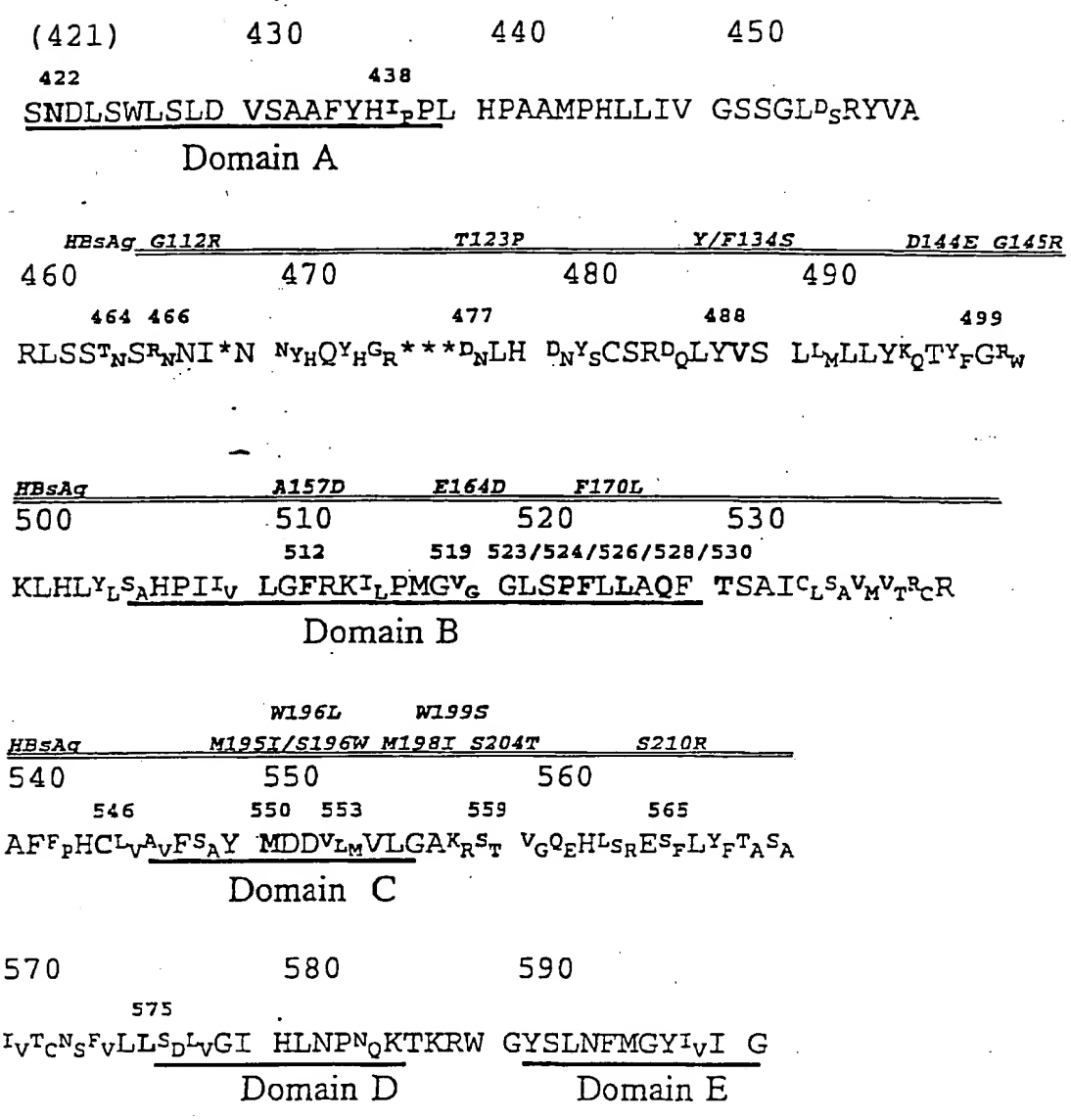
B Domain
HBV POL
HBsAg
I526M
no change
C Domain
HBV POL
HBsAg
M550I
W196S/L
HBV POL
HBsAg
M550V
I195M
D15G
D16E
Q182K
S155P/T
P130T or
A131P
S87G
I97L
I59T
L60V
P5T or
V13A/L
G1896A and/or
G1899A
A1762T and
G1764A
BCP/
EN II
core
pre-pre
X

Figure 1B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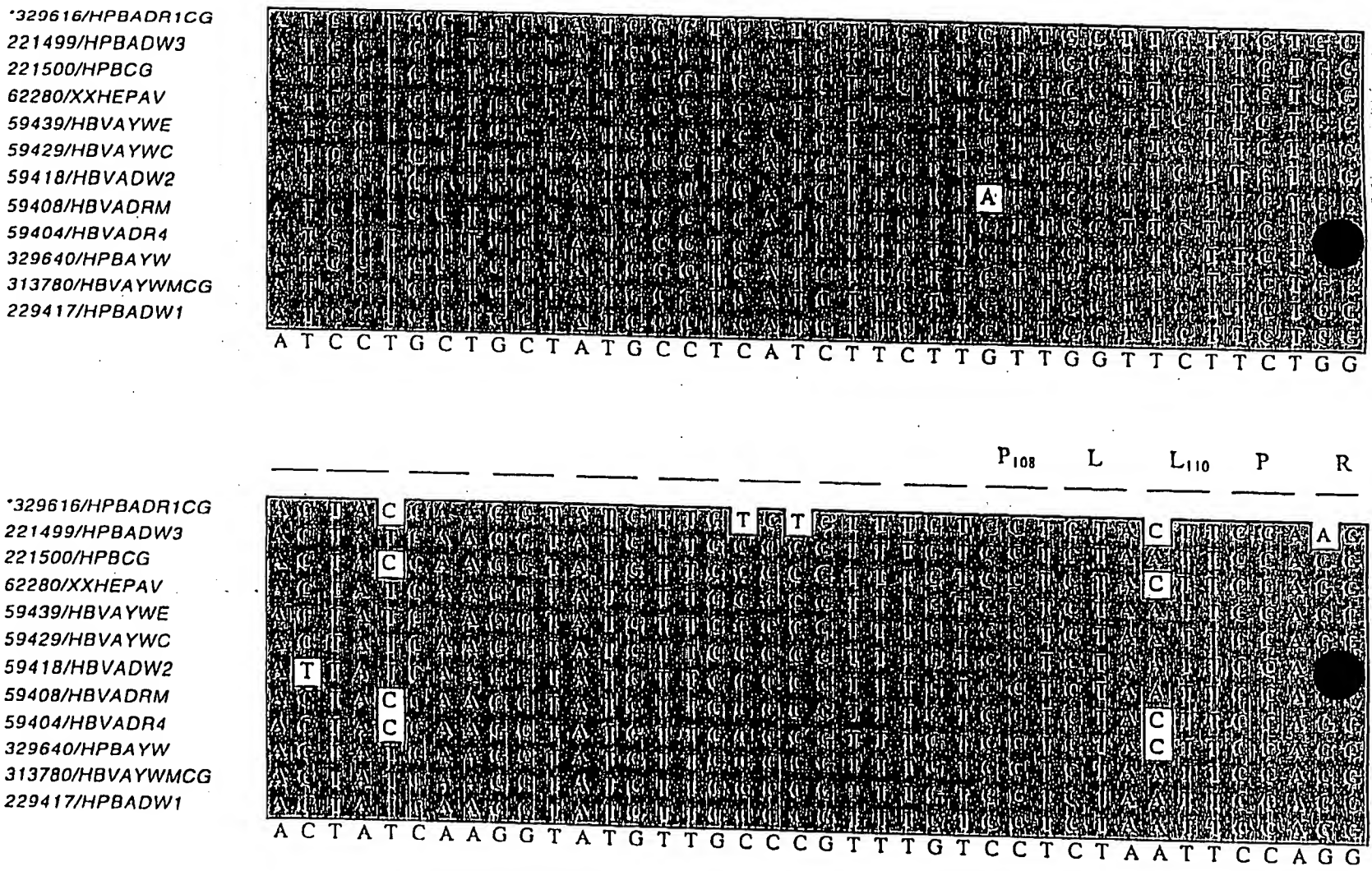
464 466 477 488 499
RLSSTNSRNNI*N NYHQYHGR***DNLH DNYSCSRDQLYVS LLMLLYKQTYFGRW
HBsAg A157D E164D F170L
500 510 520 530
512 519 523/524/526/528/530
KLHLYLSAHPIIV LGFRKILPMGVG GLSPFLLAQF TSAICLSAVMVTRCR
Domain B
W196L W199S
HBsAg M195I/S196W M198I S204T S210R
540 550 560
546 550 553 559 565
AFFPHCLVAVFSAY MDDVLMVLGAKRST VGQEHLSREFLYFTASA
Domain C
570 580 590
575
IVTCNSFVLLLSDLVGI HLNPNQKTKRW GYSLNFMGYIVI G
Domain D
Domain E

Figure 2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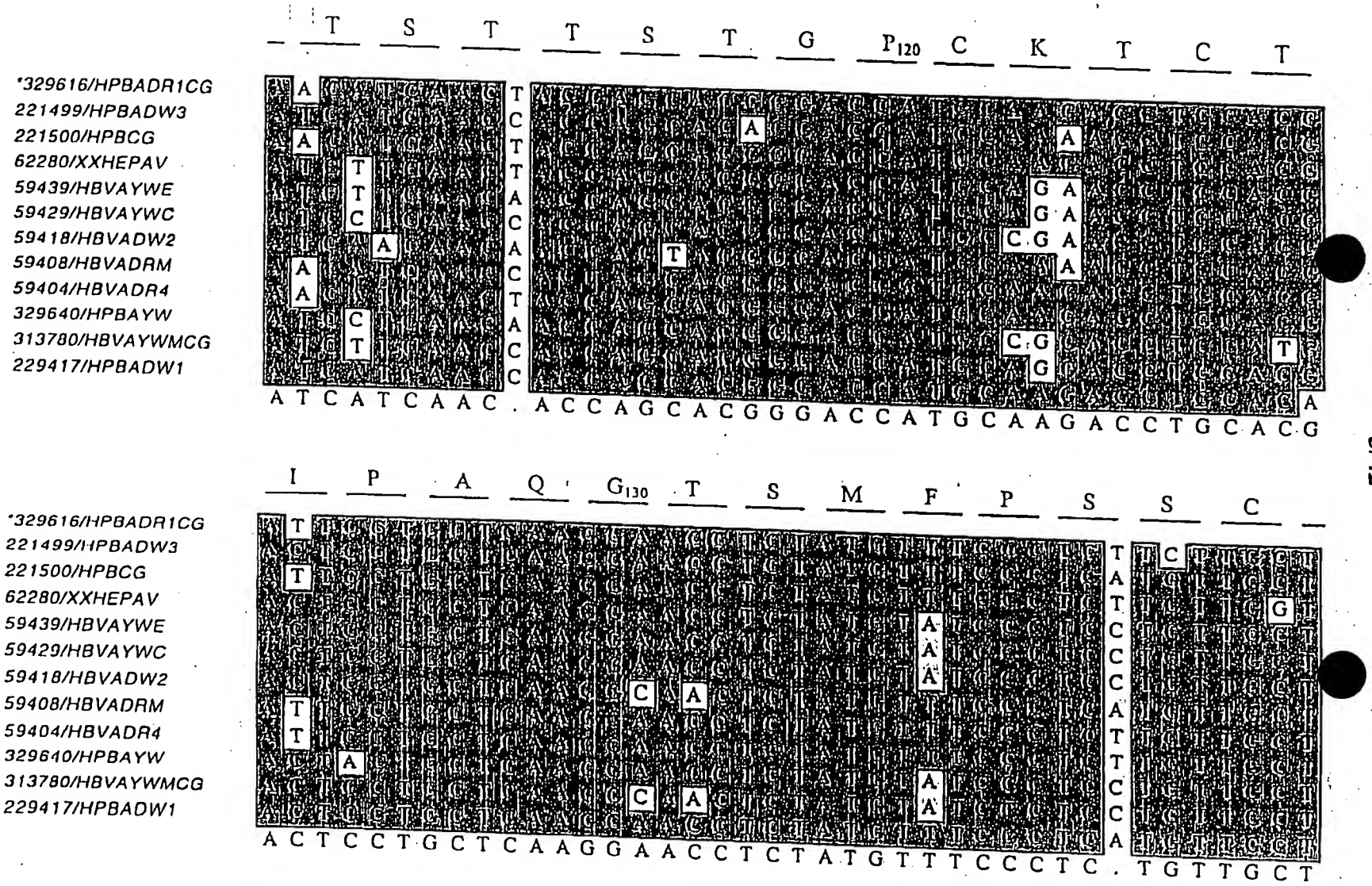
59408/HBVADRM
59404/HBVADR4
329640/HPBAYW
313780/HBVAYWMCG
229417/HPBADW1
A T C C T G C T G C T A T G C C T C A T C T T C T T G T T G G T T C T T C T G G
P108
L
L110
P
R
A C T A T C A A G G T A T G T T G C C C G T T T G T C C T C T A A T T C C A G G

Figure 3



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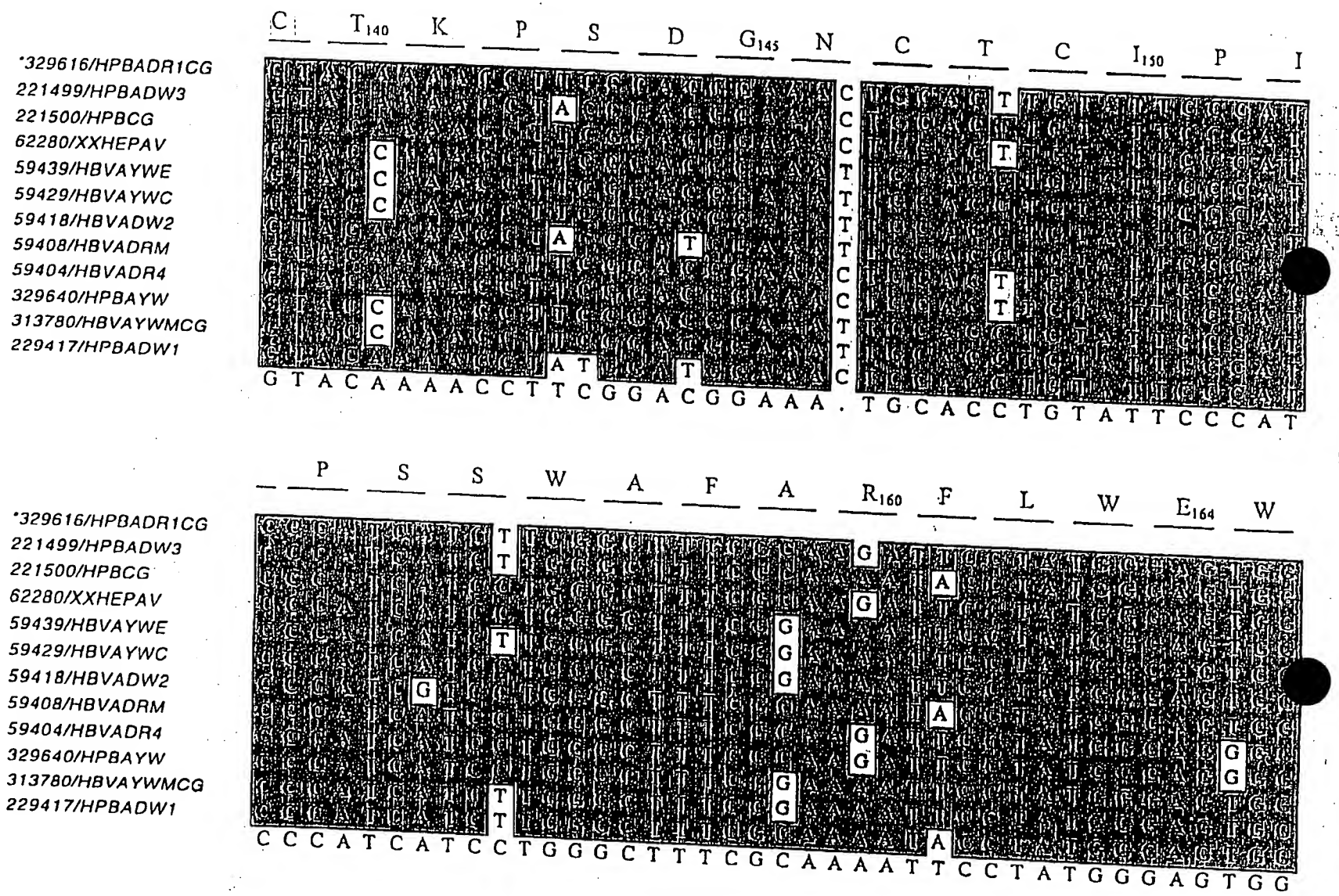


Figure 3 continued

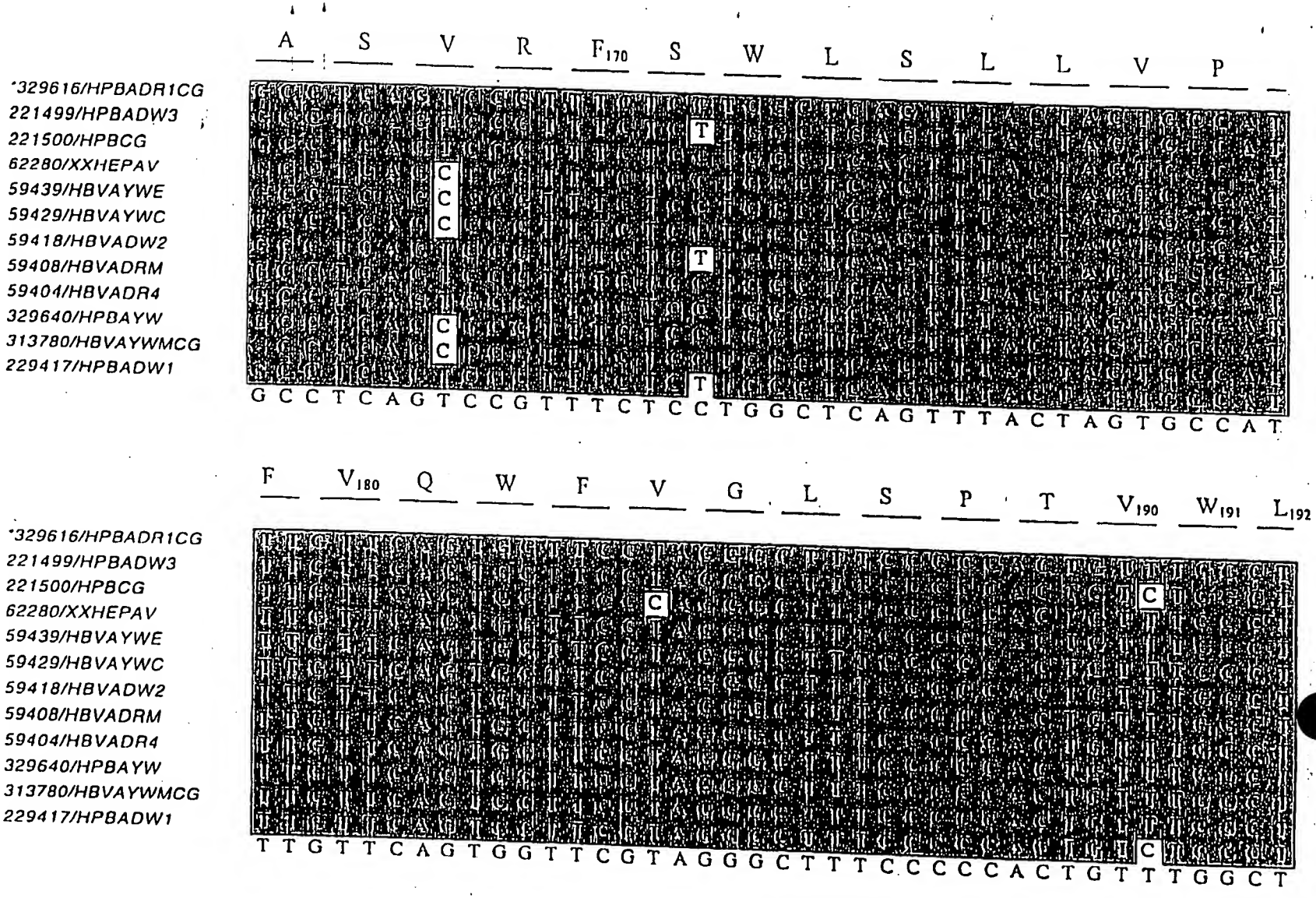


Figure 3 continued

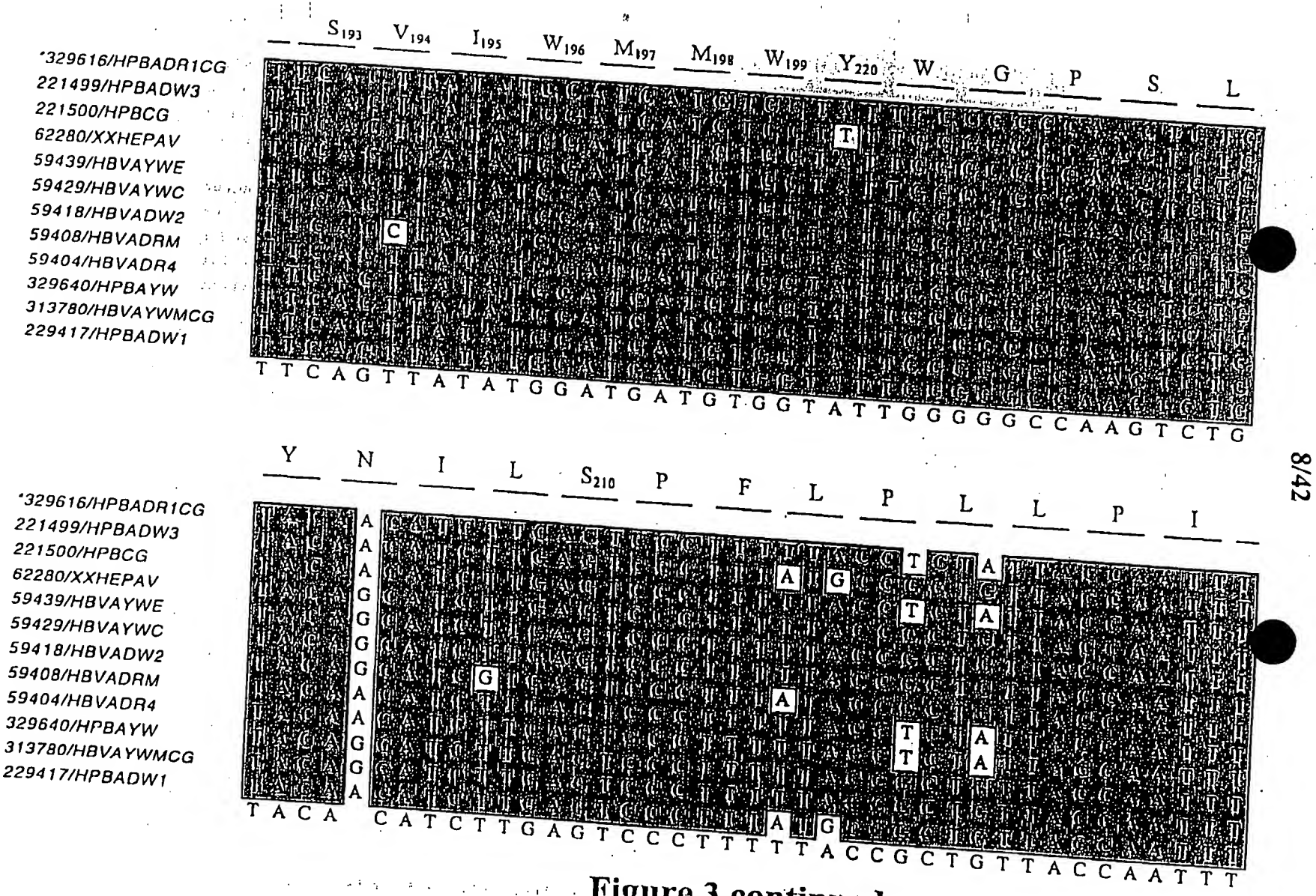


Figure 3 continued

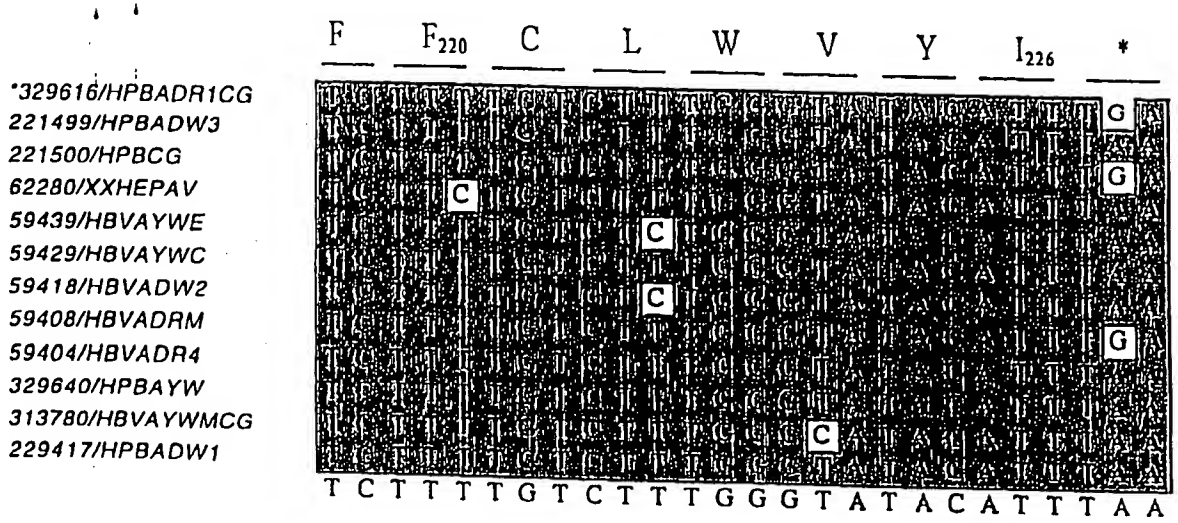
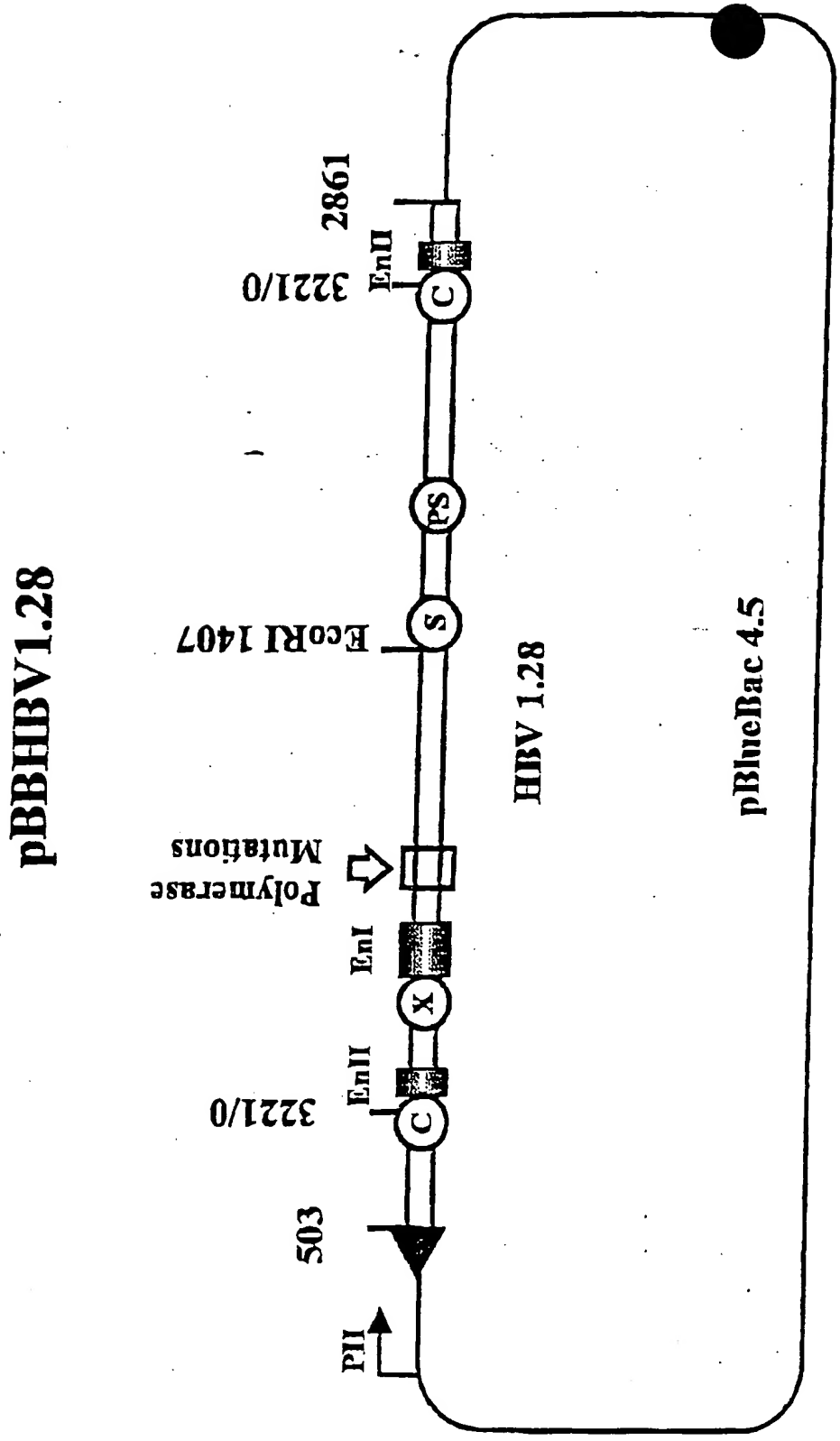


Figure 3 continued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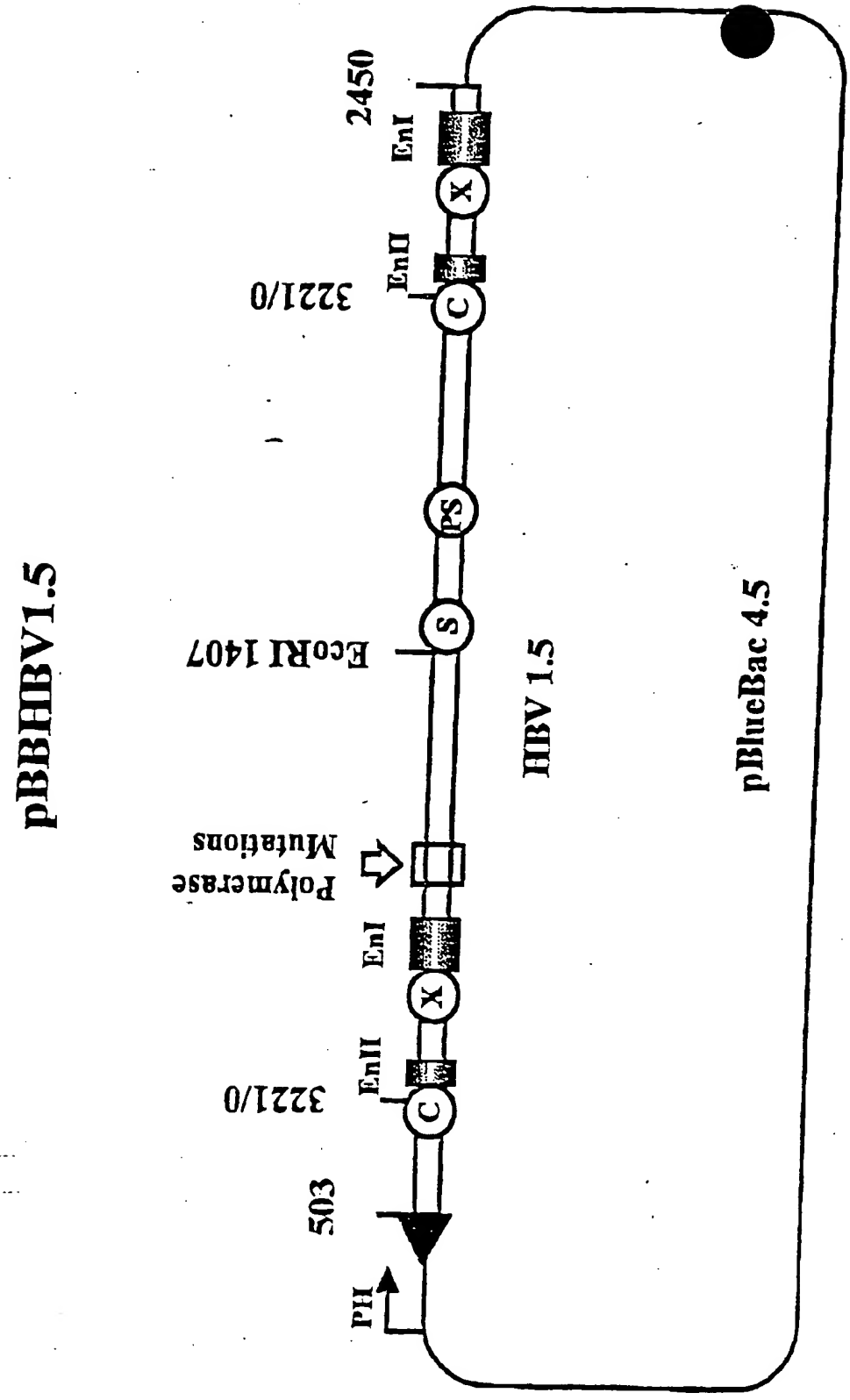
HBV 1.28
2861
EnII
3221/0
C
PS
S
EcoRI 1407
Polymerase
Mutations
EnI
X
EnII
3221/0
C
503
PII

Figure 4A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HBV 1.5
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503
3221/0
EcoRI
X
EcoRI
Polymerase
Mutations
EcoRI 1407
S
PS
3221/0
EcoRI
X
EcoRI
2450

Figure 4B

Sequence Range: 1 to 4084

```
          10         20         30         40         50
GGACGACCCCTCGCGGGGCCGCTTGGGACTCTCTCGTCCCCTTCTCCGTC

          60         70         80         90        100
TGCCGTTCCAGCCGACCACGGGGCGCACCTCTCTTTACGCGGTCTCCCCG

         110        120        130        140        150
TCTGTGCCTTCTCATCTGCCGGTCCGTGTGCACTTCGCTTCACCTCTGCA

         160        170        180        190        200
CGTTGCATGGAGACCACCGTGAACGCCCATCAGATCCTGCCCAAGGTCTT

         210        220        230        240        250
ACATAAGAGGACTCTTGGACTCCCAGCAATGTCAACGACCGACCTTGAGG

         260        270        280        290        300
CCTACTTCAAAGACTGTGTGTTTAAGGACTGGGAGGAGCTGGGGGAGGAG

         310        320        330        340        350
ATTAGGTTAAAGGTCTTTGTATTAGGAGGCTGTAGGCATAAATTGGTCTG

         360        370        380        390        400
CGCACCAGCACCATGCAACTTTTTCACCTCTGCCTAATCATCTCTTGTAC

         410        420        430        440        450
ATGTCCCACTGTTCAAGCCTCCAAGCTGTGCCTTGGGTGGCTTTGGGGCA

         460        470        480        490        500
TGGACATTGACCCTTATAAAGAATTTGGAGCTACTGTGGAGTTACTCTCG

         510        520        530        540        550
TTTTTGCCTTCTGACTTCTTTCCTTCCGTCAGAGATCTCCTAGACACCGC

         560        570        580        590        600
CTCAGCTCTGTATCGAGAAGCCTTAGAGTCTCCTGAGCATTGCTCACCTC

         610        620        630        640        650
ACCATACTGCACTCAGGCAAGCCATTCTCTGCTGGGGGGAATTGATGACT

         660        670        680        690        700
CTAGCTACCTGGGTGGGTAATAATTTGGAAGATCCAGCATCCAGGGATCT
```

Figure 5A

```
       710        720        730        740        750
AGTAGTCAATTATGTTAATACTAACATGGGTTTAAAGATCAGGCAACTAT

       760        770        780        790        800
TGTGGTTTCATATATCTTGCCTTACTTTTGGAAGAGAGACTGTACTTGAA

       810        820        830        840        850
TATTTGGTCTCTTTCGGAGTGTGGATTCGCACTCCTCCAGCCTATAGACC

       860        870        880        890        900
ACCAAATGCCCCTATCTTATCAACACTTCCGGAAACTACTGTTGTTAGAC

       910        920        930        940        950
GACGGGACCGAGGCAGGTCCCCTAGAAGAAGAACTCCCTCGCCTCGCAGA

       960        970        980        990       1000
CGCAGATCTCAATCGCCGCGTCGCAGAAGATCTCAATCTCGGGAATCTCA

      1010       1020       1030       1040       1050
ATGTTAGTATTCCTTGGACTCATAAGGTGGGAAACTTTACGGGGCTTTAT

      1060       1070       1080       1090       1100
TCCTCTACAGTACCTATCTTTAATCCTGAATGGCAAACTCCTTCCTTTCC

      1110       1120       1130       1140       1150
TAAGATTCATTTACAAGAGGACATTATTAATAGGTGTCAACAATTTGTGG

      1160       1170       1180       1190       1200
GCCCTCTCACTGTAAATGAAAAGAGAAGATTGAAATTAATTATGCCTGCT

      1210       1220       1230       1240       1250
AGATTCTATCCTACCCACACTAAATATTTGCCCTTAGACAAAGGAATTAA

      1260       1270       1280       1290       1300
ACCTTATTATCCAGATCAGGTAGTTAATCATTACTTCCAAACCAGACATT

      1310       1320       1330       1340       1350
ATTTACATACTCTTTGGAAGGCTGGTATTCTATATAAGAGGGAAACCACA

      1360       1370       1380       1390       1400
CGTAGCGCATCATTTTGCGGGTCACCATATTCTTGGGAACAAGAGCTACA

      1410       1420       1430       1440       1450
GCATGGGAGGTTGGTCATCAAAACCTCGCAAAGGCATGGGGACGAATCTT
```

Figure 5A continued

```
      1460       1470       1480       1490       1500
TCTGTTCCCAACCCTCTGGGATTCTTTCCCGATCATCAGTTGGACCCTGC

      1510       1520       1530       1540       1550
ATTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCATCAAGG

      1560       1570       1580       1590       1600
ACCACTGGCCAGCAGCCAACCAGGTAGGAGTGGGAGCATTCGGGCCAGGG

      1610       1620       1630       1640       1650
CTCACCCCTCCACACGGCGGTATTTTGGGGTGGAGCCCTCAGGCTCAGGG

      1660       1670       1680       1690       1700
CATATTGACCACAGTGTCAACAATTCCTCCTCCTGCCTCCACCAATCGGC

      1710       1720       1730       1740       1750
AGTCAGGAAGGCAGCCTACTCCCATCTCTCCACCTCTAAGAGACAGTCAT

      1760       1770       1780       1790       1800
CCTCAGGCCATGCAGTGGAATTCCACTGCCTTCCACCAAGCTCTGCAGGA

      1810       1820       1830       1840       1850
TCCCAGAGTCAGGGGTCTGTATCTTCCTGCTGGTGGCTCCAGTTCAGGAA

      1860       1870       1880       1890       1900
CAGTAAACCCTGCTCCGAATATTGCCTCTCACATCTCGTCAATCTCCGCG

      1910       1920       1930       1940       1950
AGGACTGGGGACCCTGTGACGAACATGGAGAACATCACATCAGGATTCCT

      1960       1970       1980       1990       2000
AGGACCCCTGCTCGTGTTACAGGCGGGGTTTTTCTTGTTGACAAGAATCC

      2010       2020       2030       2040       2050
TCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTA

      2060       2070       2080       2090       2100
GGGGGATCTCCCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAA

      2110       2120       2130       2140       2150
TCACTCACCAACCTCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGT

      2160       2170       2180       2190       2200
GTCTGCGGCGTTTTATCATATTCCTCTTCATCCTGCTGCTATGCCTCATC
```

Figure 5A continued

```
      2210       2220       2230       2240       2250
TTCTTATTGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCCTCT

      2260       2270       2280       2290       2300
AATTCCAGGATCAACAACAACCAGTACGGGACCATGCAAAACCTGCACGA

      2310       2320       2330       2340       2350
CTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCT

      2360       2370       2380       2390       2400
ACGGATGGAAATTGCACCTGTATTCCCATCCCATCGTCCTGGGCTTTCGC

      2410       2420       2430       2440       2450
AAAATACCTATGGGAGTGGGCCTCAGTCCGTTTCTCTTGGCTCAGTTTAC

      2460       2470       2480       2490       2500
TAGTGCCATTTGTTCAGTGGTTCGTAGGGCTTTCCCCCACTGTTTGGCTT

      2510       2520       2530       2540       2550
TCAGCTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAGCATCGT

      2560       2570       2580       2590       2600
GAGTCCCTTTATACCGCTGTTACCAATTTTCTTTTGTCTCTGGGTATACA

      2610       2620       2630       2640       2650
TTTAAACCCTAACAAAACAAAAAGATGGGGTTATTCCCTAAACTTCATGG

      2660       2670       2680       2690       2700
GCTACATAATTGGAAGTTGGGGAACTTTGCCACAGGATCATATTGTACAA

      2710       2720       2730       2740       2750
AAGATCAAACACTGTTTTAGAAAACTTCCTGTTAACAGGCCTATTGATTG

      2760       2770       2780       2790       2800
GAAAGTATGTCAAAGAATTGTGGGTCTTTTGGGCTTTGCTGCTCCATTTA

      2810       2820       2830       2840       2850
CACAATGTGGATATCCTGCCTTAATGCCTTTGTATGCATGTATACAAGCT

      2860       2870       2880       2890       2900
AAACAGGCTTTCACTTTCTCGCCAACTTACAAGGCCTTTCTAAGTAAACA

      2910       2920       2930       2940       2950
GTACATGAACCTTTACCCCGTTGCTCGGCAACGGCCTGGTCTGTGCCAAG
```

Figure 5A continued

```
2960       2970       2980       2990       3000
TGTTTGCTGACGCAACCCCCACTGGCTGGGGCTTGGCCATAGGCCATCAG

3010       3020       3030       3040       3050
CGCATGCGTGGAACCTTTGTGGCTCCTCTGCCGATCCATACTGCGGAACT

3060       3070       3080       3090       3100
CCTAGCCGCTTGTTTTGCTCGCAGCCGGTCTGGAGCAAAGCTCATCGGAA

3110       3120       3130       3140       3150
CTGACAATTCTGTCGTCCTCTCGCGGAAATATACATCGTTTCCATGGCTG

3160       3170       3180       3190       3200
CTAGGCTGTACTGCCAACTGGATCCTTCGCGGGACGTCCTTTGTTTACGT

3210       3220       3230       3240       3250
CCCGTCGGCGCTGAATCCCGCGGACGACCCCTCGCGGGGCCGCTTGGGAC

3260       3270       3280       3290       3300
TCTCTCGTCCCCTTCTCCGTCTGCCGTTCCAGCCGACCACGGGGCGCACC

3310       3320       3330       3340       3350
TCTCTTTACGCGGTCTCCCCGTCTGTGCCTTCTCATCTGCCGGTCCGTGT

3360       3370       3380       3390       3400
GCACTTCGCTTCACCTCTGCACGTTGCATGGAGACCACCGTGAACGCCCA

3410       3420       3430       3440       3450
TCAGATCCTGCCCAAGGTCTTACATAAGAGGACTCTTGGACTCCCAGCAA

3460       3470       3480       3490       3500
TGTCAACGACCGACCTTGAGGCCTACTTCAAAGACTGTGTGTTTAAGGAC

3510       3520       3530       3540       3550
TGGGAGGAGCTGGGGGAGGAGATTAGGTTAAAGGTCTTTGTATTAGGAGG

3560       3570       3580       3590       3600
CTGTAGGCATAAATTGGTCTGCGCACCAGCACCATGCAACTTTTTCACCT

3610       3620       3630       3640       3650
CTGCCTAATCATCTCTTGTACATGTCCCACTGTTCAAGCCTCCAAGCTGT

3660       3670       3680       3690       3700
GCCTTGGGTGGCTTTGGGGCATGGACATTGACCCTTATAAAGAATTTGGA
```

Figure 5A continued

```
      3710       3720       3730       3740       3750
GCTACTGTGGAGTTACTCTCGTTTTTGCCTTCTGACTTCTTTCCTTCCGT

      3760       3770       3780       3790       3800
CAGAGATCTCCTAGACACCGCCTCAGCTCTGTATCGAGAAGCCTTAGAGT

      3810       3820       3830       3840       3850
CTCCTGAGCATTGCTCACCTCACCATACTGCACTCAGGCAAGCCATTCTC

      3860       3870       3880       3890       3900
TGCTGGGGGGAATTGATGACTCTAGCTACCTGGGTGGGTAATAATTTGGA

      3910       3920       3930       3940       3950
AGATCCAGCATCCAGGGATCTAGTAGTCAATTATGTTAATACTAACATGG

      3960       3970       3980       3990       4000
GTTTAAAGATCAGGCAACTATTGTGGTTTCATATATCTTGCCTTACTTTT

      4010       4020       4030       4040       4050
GGAAGAGAGACTGTACTTGAATATTTGGTCTCTTTCGGAGTGTGGATTCG

      4060       4070       4080
CACTCCTCCAGCCTATAGACCACCAAATGCCCCT
```

Figure 5A continued

Sequence Range: 1 to 4496

```
          10         20         30         40         50
GATATCCTGCCTTAATGCCTTTGTATGCATGTATACAAGCTAAACAGGCT

          60         70         80         90        100
TTCACTTTCTCGCCAACTTACAAGGCCTTTCTAAGTAAACAGTACATGAA

         110        120        130        140        150
CCTTTACCCCGTTGCTCGGCAACGGCCTGGTCTGTGCCAAGTGTTTGCTG

         160        170        180        190        200
ACGCAACCCCCACTGGCTGGGGCTTGGCCATAGGCCATCAGCGCATGCGT

         210        220        230        240        250
GGAACCTTTGTGGCTCCTCTGCCGATCCATACTGCGGAACTCCTAGCCGC

         260        270        280        290        300
TTGTTTTGCTCGCAGCCGGTCTGGAGCAAAGCTCATCGGAACTGACAATT

         310        320        330        340        350
CTGTCGTCCTCTCGCGGAAATATACATCGTTTCCATGGCTGCTAGGCTGT

         360        370        380        390        400
ACTGCCAACTGGATCCTTCGCGGGACGTCCTTTGTTTACGTCCCGTCGGC

         410        420        430        440        450
GCTGAATCCCGCGGACGACCCCTCGCGGGGCCGCTTGGGACTCTCTCGTC

         460        470        480        490        500
CCCTTCTCCGTCTGCCGTTCCAGCCGACCACGGGGCGCACCTCTCTTTAC

         510        520        530        540        550
GCGGTCTCCCCGTCTGTGCCTTCTCATCTGCCGGTCCGTGTGCACTTCGC

         560        570        580        590        600
TTCACCTCTGCACGTTGCATGGAGACCACCGTGAACGCCCATCAGATCCT

         610        620        630        640        650
GCCCAAGGTCTTACATAAGAGGACTCTTGGACTCCCAGCAATGTCAACGA

         660        670        680        690        700
CCGACCTTGAGGCCTACTTCAAAGACTGTGTGTTTAAGGACTGGGAGGAG
```

Figure 5B

```
       710        720        730        740        750
CTGGGGGAGGAGATTAGGTTAAAGGTCTTTGTATTAGGAGGCTGTAGGCA

       760        770        780        790        800
TAAATTGGTCTGCGCACCAGCACCATGCAACTTTTTCACCTCTGCCTAAT

       810        820        830        840        850
CATCTCTTGTACATGTCCCACTGTTCAAGCCTCCAAGCTGTGCCTTGGGT

       860        870        880        890        900
GGCTTTGGGGCATGGACATTGACCCTTATAAAGAATTTGGAGCTACTGTG

       910        920        930        940        950
GAGTTACTCTCGTTTTTGCCTTCTGACTTCTTTCCTTCCGTCAGAGATCT

       960        970        980        990       1000
CCTAGACACCGCCTCAGCTCTGTATCGAGAAGCCTTAGAGTCTCCTGAGC

      1010       1020       1030       1040       1050
ATTGCTCACCTCACCATACTGCACTCAGGCAAGCCATTCTCTGCTGGGGG

      1060       1070       1080       1090       1100
GAATTGATGACTCTAGCTACCTGGGTGGGTAATAATTTGGAAGATCCAGC

      1110       1120       1130       1140       1150
ATCCAGGGATCTAGTAGTCAATTATGTTAATACTAACATGGGTTTAAAGA

      1160       1170       1180       1190       1200
TCAGGCAACTATTGTGGTTTCATATATCTTGCCTTACTTTTGGAAGAGAG

      1210       1220       1230       1240       1250
ACTGTACTTGAATATTTGGTCTCTTTCGGAGTGTGGATTCGCACTCCTCC

      1260       1270       1280       1290       1300
AGCCTATAGACCACCAAATGCCCCTATCTTATCAACACTTCCGGAAACTA

      1310       1320       1330       1340       1350
CTGTTGTTAGACGACGGGACCGAGGCAGGTCCCCTAGAAGAAGAACTCCC

      1360       1370       1380       1390       1400
TCGCCTCGCAGACGCAGATCTCAATCGCCGCGTCGCAGAAGATCTCAATC

      1410       1420       1430       1440       1450
TCGGGAATCTCAATGTTAGTATTCCTTGGACTCATAAGGTGGGAAACTTT
```

Figure 5B continued

```
      1460       1470       1480       1490       1500
ACGGGGCTTTATTCCTCTACAGTACCTATCTTTAATCCTGAATGGCAAAC

      1510       1520       1530       1540       1550
TCCTTCCTTTCCTAAGATTCATTTACAAGAGGACATTATTAATAGGTGTC

      1560       1570       1580       1590       1600
AACAATTTGTGGGCCCTCTCACTGTAAATGAAAAGAGAAGATTGAAATTA

      1610       1620       1630       1640       1650
ATTATGCCTGCTAGATTCTATCCTACCCACACTAAATATTTGCCCTTAGA

      1660       1670       1680       1690       1700
CAAAGGAATTAAACCTTATTATCCAGATCAGGTAGTTAATCATTACTTCC

      1710       1720       1730       1740       1750
AAACCAGACATTATTTACATACTCTTTGGAAGGCTGGTATTCTATATAAG

      1760       1770       1780       1790       1800
AGGGAAACCACACGTAGCGCATCATTTTGCGGGTCACCATATTCTTGGGA

      1810       1820       1830       1840       1850
ACAAGAGCTACAGCATGGGAGGTTGGTCATCAAAACCTCGCAAAGGCATG

      1860       1870       1880       1890       1900
GGGACGAATCTTTCTGTTCCCAACCCTCTGGGATTCTTTCCCGATCATCA

      1910       1920       1930       1940       1950
GTTGGACCCTGCATTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCA

      1960       1970       1980       1990       2000
ACCCCATCAAGGACCACTGGCCAGCAGCCAACCAGGTAGGAGTGGGAGCA

      2010       2020       2030       2040       2050
TTCGGGCCAGGGCTCACCCCTCCACACGGCGGTATTTTGGGGTGGAGCCC

      2060       2070       2080       2090       2100
TCAGGCTCAGGGCATATTGACCACAGTGTCAACAATTCCTCCTCCTGCCT

      2110       2120       2130       2140       2150
CCACCAATCGGCAGTCAGGAAGGCAGCCTACTCCCATCTCTCCACCTCTA

      2160       2170       2180       2190       2200
AGAGACAGTCATCCTCAGGCCATGCAGTGGAATTCCACTGCCTTCCACCA
```

Figure 5B continued

```
      2210       2220       2230       2240       2250
AGCTCTGCAGGATCCCAGAGTCAGGGGTCTGTATCTTCCTGCTGGTGGCT

      2260       2270       2280       2290       2300
CCAGTTCAGGAACAGTAAACCCTGCTCCGAATATTGCCTCTCACATCTCG

      2310       2320       2330       2340       2350
TCAATCTCCGCGAGGACTGGGGACCCTGTGACGAACATGGAGAACATCAC

      2360       2370       2380       2390       2400
ATCAGGATTCCTAGGACCCCTGCTCGTGTTACAGGCGGGGTTTTTCTTGT

      2410       2420       2430       2440       2450
TGACAAGAATCCTCACAATACCGCAGAGTCTAGACTCGTGGTGGACTTCT

      2460       2470       2480       2490       2500
CTCAATTTTCTAGGGGGATCTCCCGTGTGTCTTGGCCAAAATTCGCAGTC

      2510       2520       2530       2540       2550
CCCAACCTCCAATCACTCACCAACCTCCTGTCCTCCAATTTGTCCTGGTT

      2560       2570       2580       2590       2600
ATCGCTGGATGTGTCTGCGGCGTTTTATCATATTCCTCTTCATCCTGCTG

      2610       2620       2630       2640       2650
CTATGCCTCATCTTCTTATTGGTTCTTCTGGATTATCAAGGTATGTTGCC

      2660       2670       2680       2690       2700
CGTTTGTCCTCTAATTCCAGGATCAACAACAACCAGTACGGGACCATGCA

      2710       2720       2730       2740       2750
AAACCTGCACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGC

      2760       2770       2780       2790       2800
TGTACAAAACCTACGGATGGAAATTGCACCTGTATTCCCATCCCATCGTC

      2810       2820       2830       2840       2850
CTGGGCTTTCGCAAAATACCTATGGGAGTGGGCCTCAGTCCGTTTCTCTT

      2860       2870       2880       2890       2900
GGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCGTAGGGCTTTCCCCC

      2910       2920       2930       2940       2950
ACTGTTTGGCTTTCAGCTATATGGATGATGTGGTATTGGGGGCCAAGTCT
```

Figure 5B continued

```
      2960       2970       2980       2990       3000
GTACAGCATCGTGAGTCCCTTTATACCGCTGTTACCAATTTTCTTTTGTC

      3010       3020       3030       3040       3050
TCTGGGTATACATTTAAACCCTAACAAAACAAAAAGATGGGGTTATTCCC

      3060       3070       3080       3090       3100
TAAACTTCATGGGCTACATAATTGGAAGTTGGGGAACTTTGCCACAGGAT

      3110       3120       3130       3140       3150
CATATTGTACAAAAGATCAAACACTGTTTTAGAAAACTTCCTGTTAACAG

      3160       3170       3180       3190       3200
GCCTATTGATTGGAAAGTATGTCAAAGAATTGTGGGTCTTTTGGGCTTTG

      3210       3220       3230       3240       3250
CTGCTCCATTTACACAATGTGGATATCCTGCCTTAATGCCTTTGTATGCA

      3260       3270       3280       3290       3300
TGTATACAAGCTAAACAGGCTTTCACTTTCTCGCCAACTTACAAGGCCTT

      3310       3320       3330       3340       3350
TCTAAGTAAACAGTACATGAACCTTTACCCCGTTGCTCGGCAACGGCCTG

      3360       3370       3380       3390       3400
GTCTGTGCCAAGTGTTTGCTGACGCAACCCCCACTGGCTGGGGCTTGGCC

      3410       3420       3430       3440       3450
ATAGGCCATCAGCGCATGCGTGGAACCTTTGTGGCTCCTCTGCCGATCCA

      3460       3470       3480       3490       3500
TACTGCGGAACTCCTAGCCGCTTGTTTTGCTCGCAGCCGGTCTGGAGCAA

      3510       3520       3530       3540       3550
AGCTCATCGGAACTGACAATTCTGTCGTCCTCTCGCGGAAATATACATCG

      3560       3570       3580       3590       3600
TTTCCATGGCTGCTAGGCTGTACTGCCAACTGGATCCTTCGCGGGACGTC

      3610       3620       3630       3640       3650
CTTTGTTTACGTCCCGTCGGCGCTGAATCCCGCGGACGACCCCTCGCGGG

      3660       3670       3680       3690       3700
GCCGCTTGGGACTCTCTCGTCCCCTTCTCCGTCTGCCGTTCCAGCCGACC
```

Figure 5B continued

```
      3710       3720       3730       3740       3750
ACGGGGCGCACCTCTCTTTACGCGGTCTCCCCGTCTGTGCCTTCTCATCT

      3760       3770       3780       3790       3800
GCCGGTCCGTGTGCACTTCGCTTCACCTCTGCACGTTGCATGGAGACCAC

      3810       3820       3830       3840       3850
CGTGAACGCCCATCAGATCCTGCCCAAGGTCTTACATAAGAGGACTCTTG

      3860       3870       3880       3890       3900
GACTCCCAGCAATGTCAACGACCGACCTTGAGGCCTACTTCAAAGACTGT

      3910       3920       3930       3940       3950
GTGTTTAAGGACTGGGAGGAGCTGGGGGAGGAGATTAGGTTAAAGGTCTT

      3960       3970       3980       3990       4000
TGTATTAGGAGGCTGTAGGCATAAATTGGTCTGCGCACCAGCACCATGCA

      4010       4020       4030       4040       4050
ACTTTTTCACCTCTGCCTAATCATCTCTTGTACATGTCCCACTGTTCAAG

      4060       4070       4080       4090       4100
CCTCCAAGCTGTGCCTTGGGTGGCTTTGGGGCATGGACATTGACCCTTAT

      4110       4120       4130       4140       4150
AAAGAATTTGGAGCTACTGTGGAGTTACTCTCGTTTTTGCCTTCTGACTT

      4160       4170       4180       4190       4200
CTTTCCTTCCGTCAGAGATCTCCTAGACACCGCCTCAGCTCTGTATCGAG

      4210       4220       4230       4240       4250
AAGCCTTAGAGTCTCCTGAGCATTGCTCACCTCACCATACTGCACTCAGG

      4260       4270       4280       4290       4300
CAAGCCATTCTCTGCTGGGGGGAATTGATGACTCTAGCTACCTGGGTGGG

      4310       4320       4330       4340       4350
TAATAATTTGGAAGATCCAGCATCCAGGGATCTAGTAGTCAATTATGTTA

      4360       4370       4380       4390       4400
ATACTAACATGGGTTTAAAGATCAGGCAACTATTGTGGTTTCATATATCT

      4410       4420       4430       4440       4450
TGCCTTACTTTTGGAAGAGAGACTGTACTTGAATATTTGGTCTCTTTCGG

      4460       4470       4480       4490
AGTGTGGATTCGCACTCCTCCAGCCTATAGACCACCAAATGCCCCT
```

Figure 5B continued

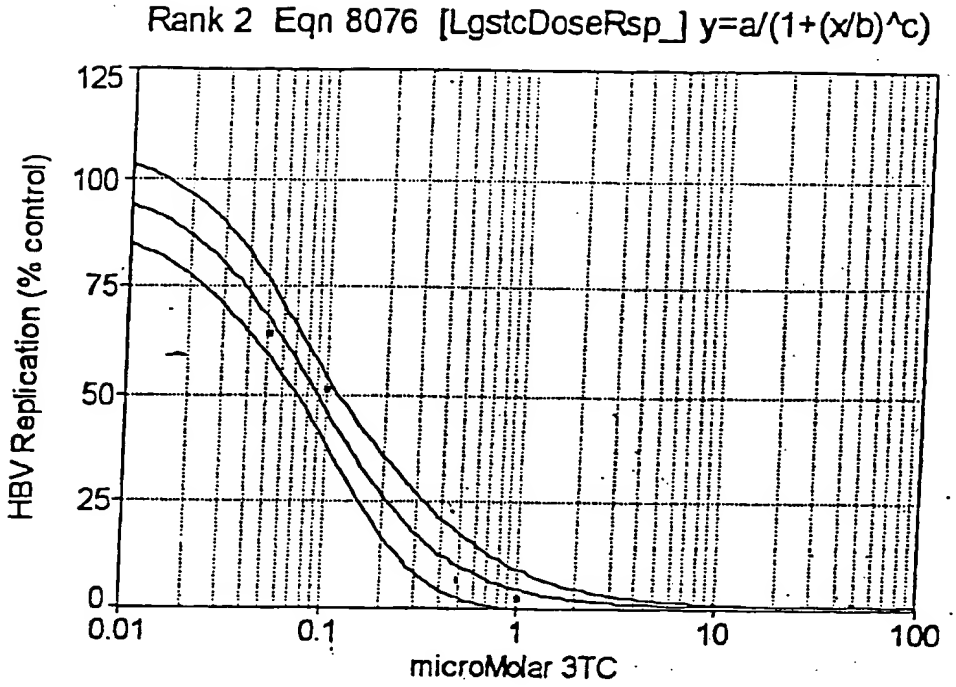


Figure 6A

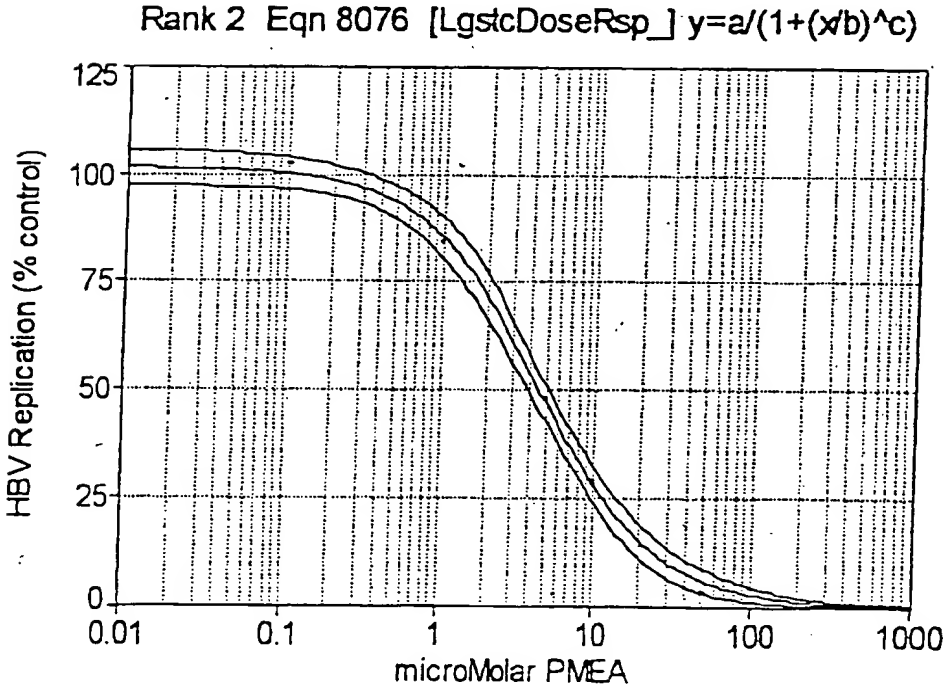


Figure 6B

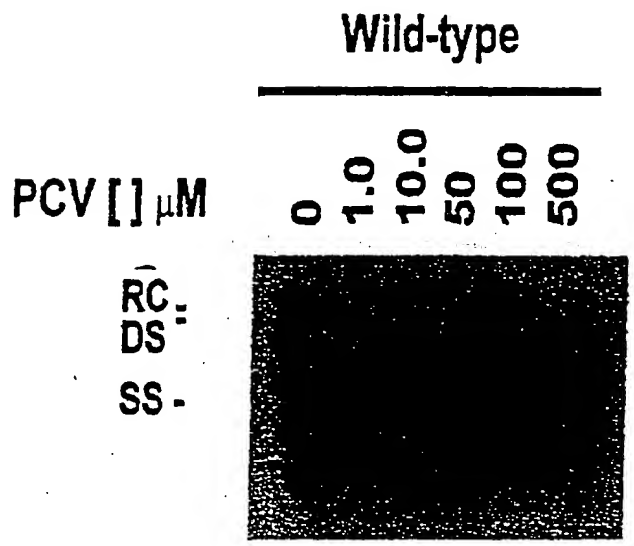


Figure 6C

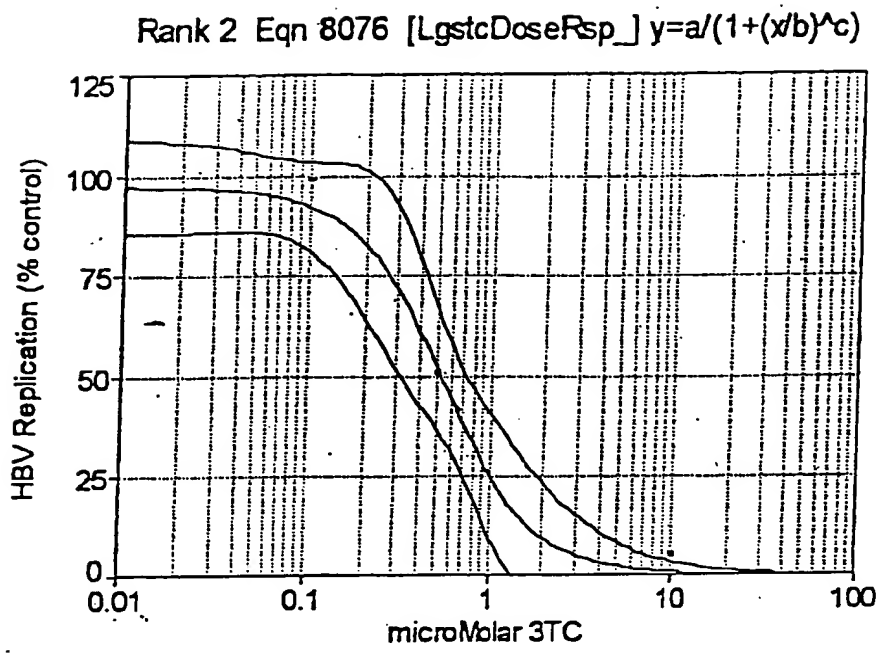


Figure 7A

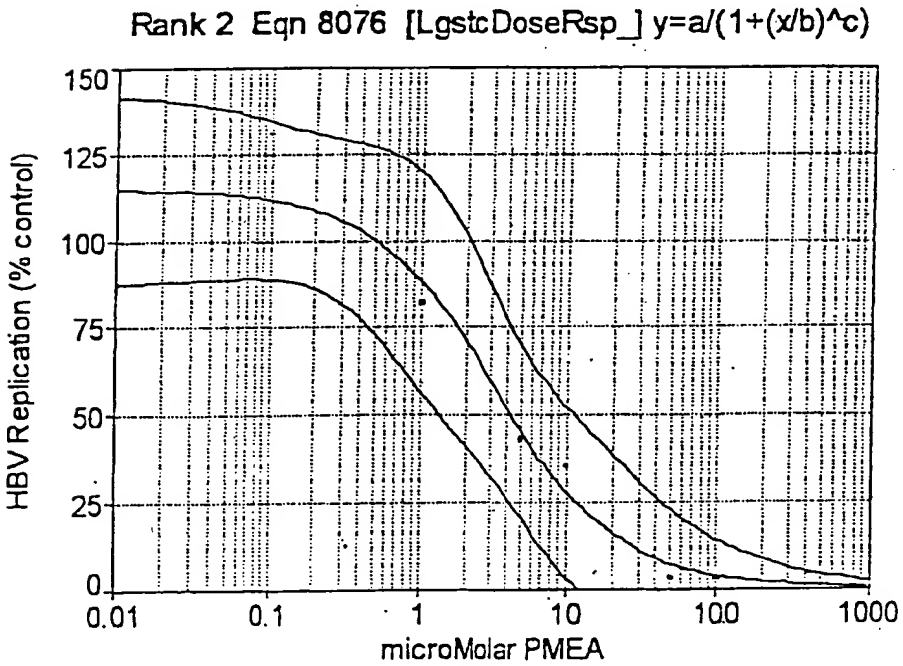


Figure 7B

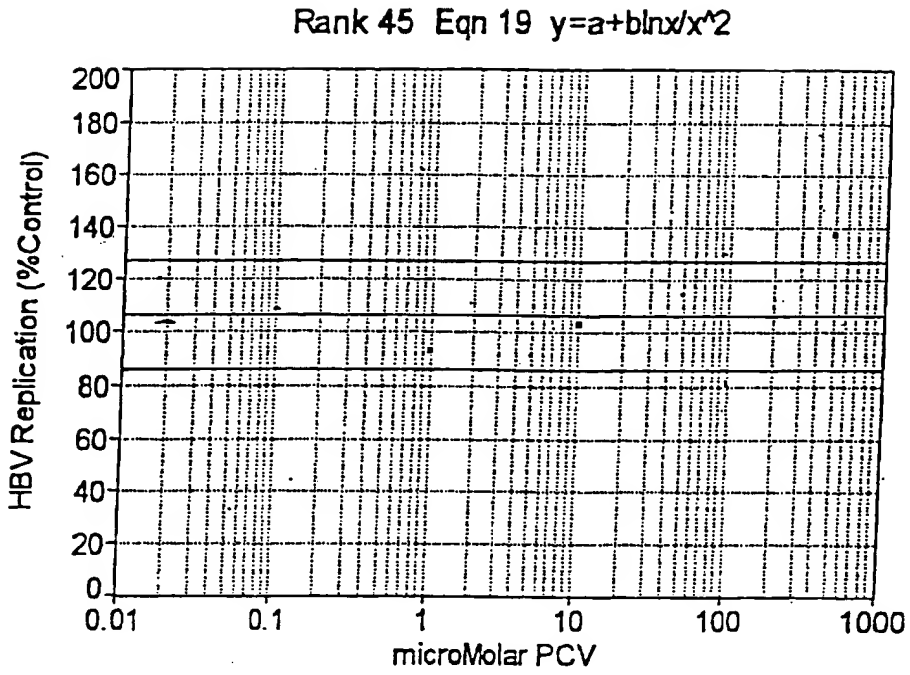

Rank 45 Eqn 19 y=a+blnx/x^2
HBV Replication (%Control)
200
180
160
140
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
microMolar PCV

Figure 7C

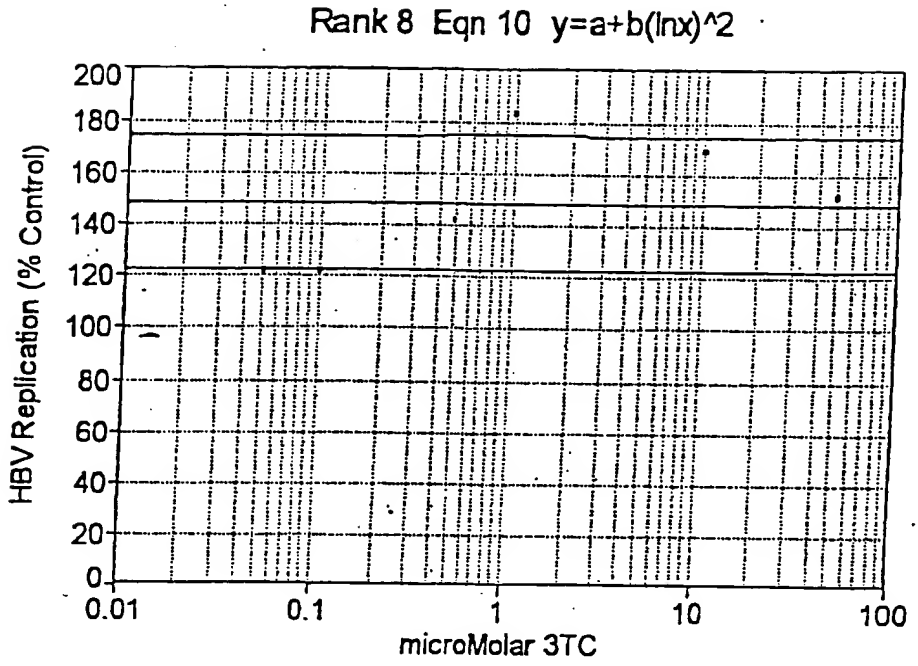


Figure 8A

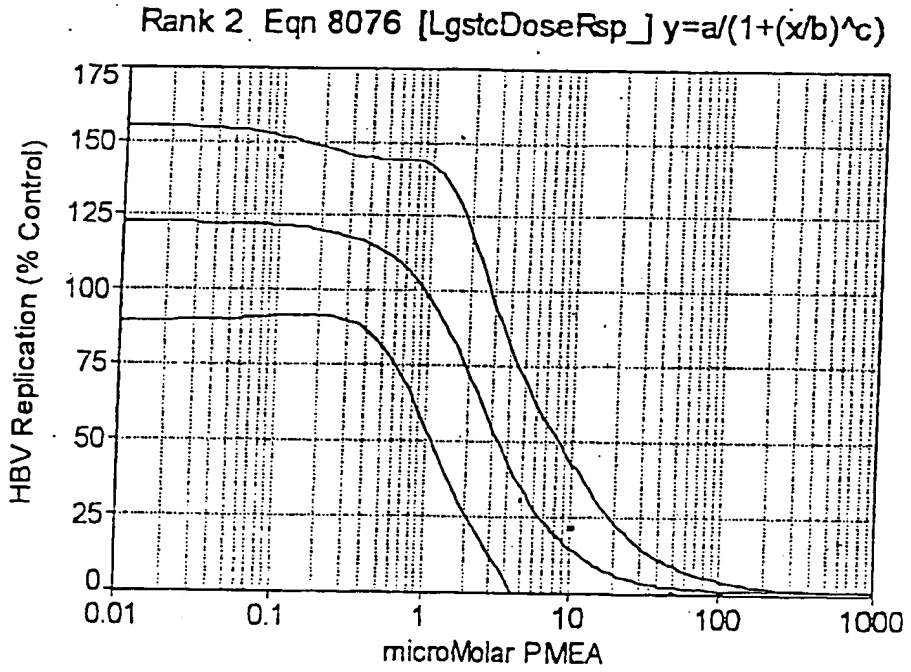


Figure 8B

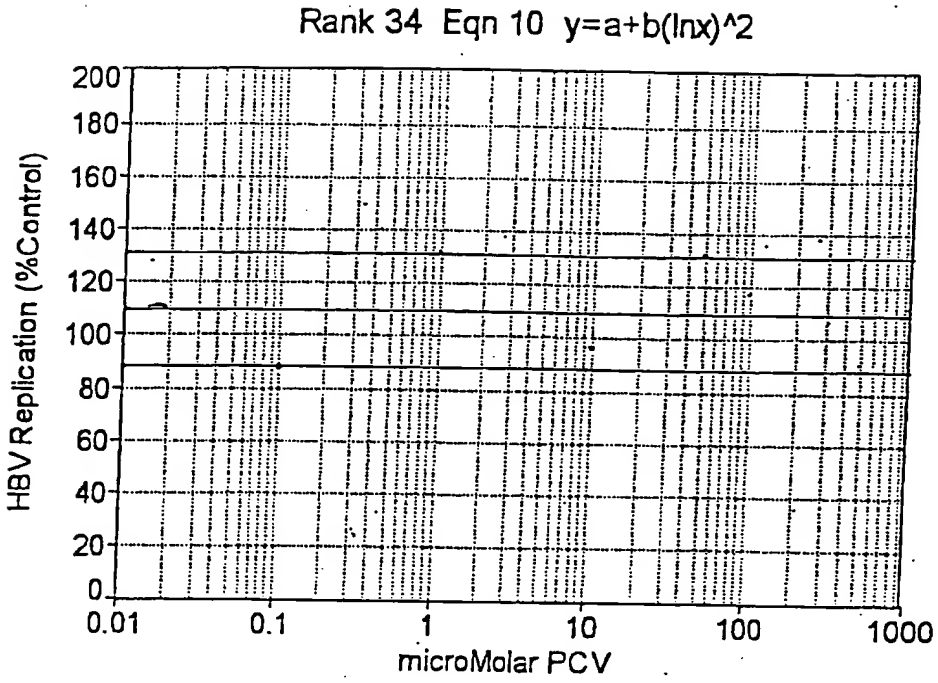

Rank 34 Eqn 10 y=a+b(lnx)^2
HBV Replication (%Control)
200
180
160
140
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
microMolar PCV

Figure 8C

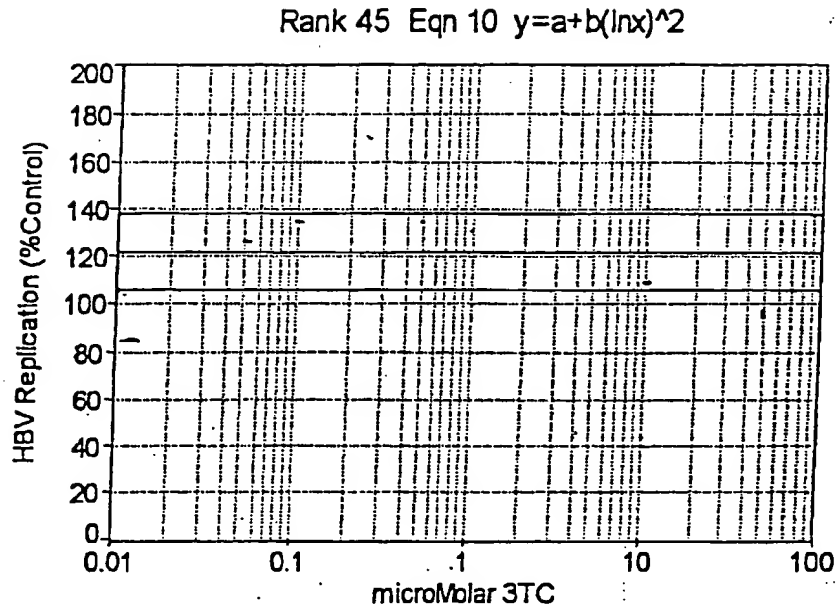


Figure 9A

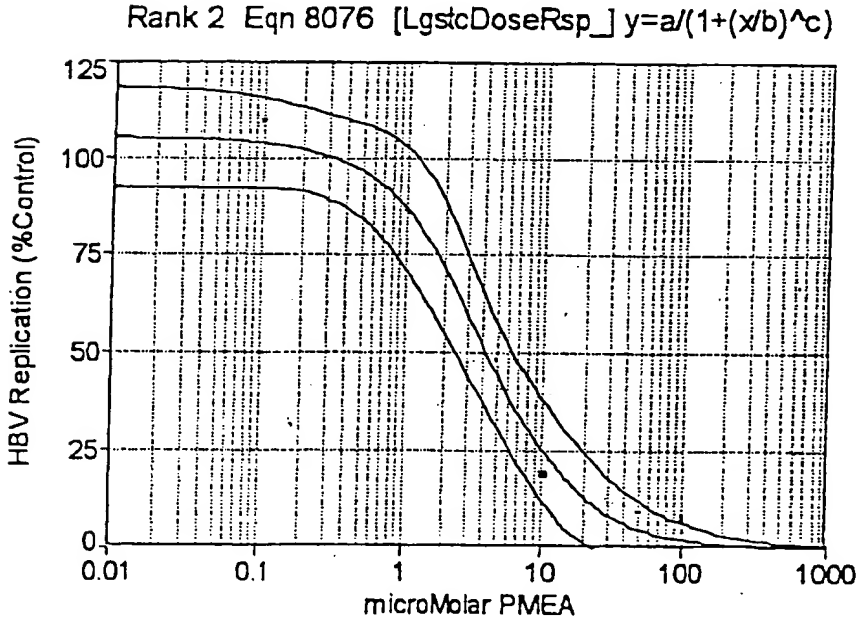


Figure 9B

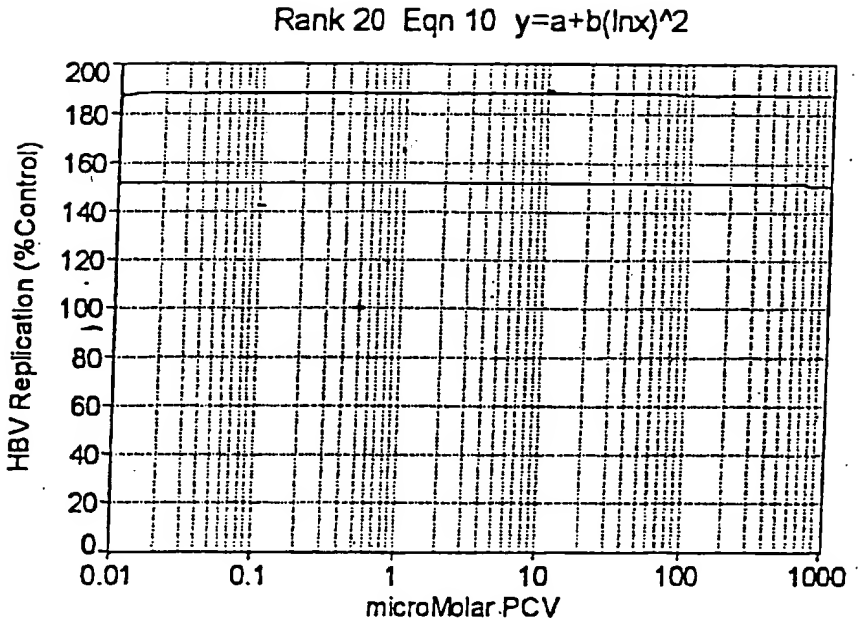

Rank 20 Eqn 10 y=a+b(lnx)^2
HBV Replication (%Control)
200
180
160
140
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
microMolar PCV

Figure 9C

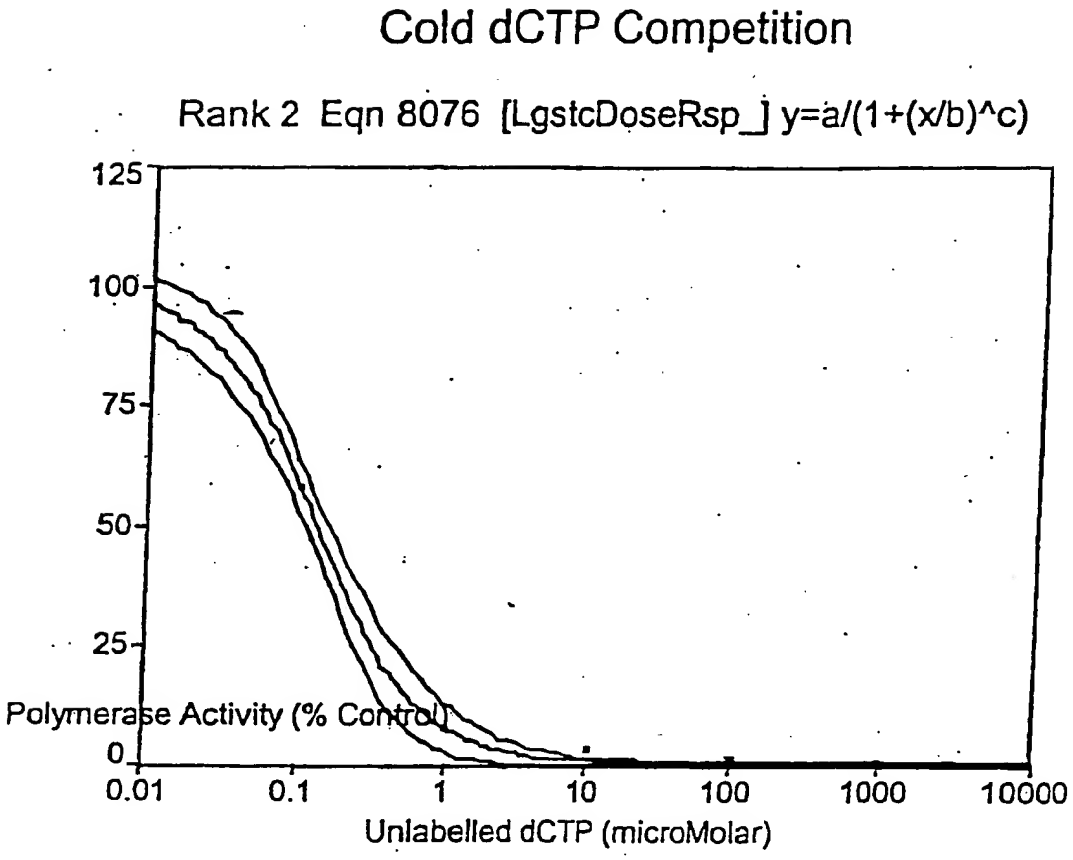

Cold dCTP Competition
Rank 2 Eqn 8076 [LgstcDoseRsp_] y=a/(1+(x/b)^c)
125
100
75
50
25
0
Polymerase Activity (% Control)
0.01
0.1
1
10
100
1000
10000
Unlabelled dCTP (microMolar)

Figure 10

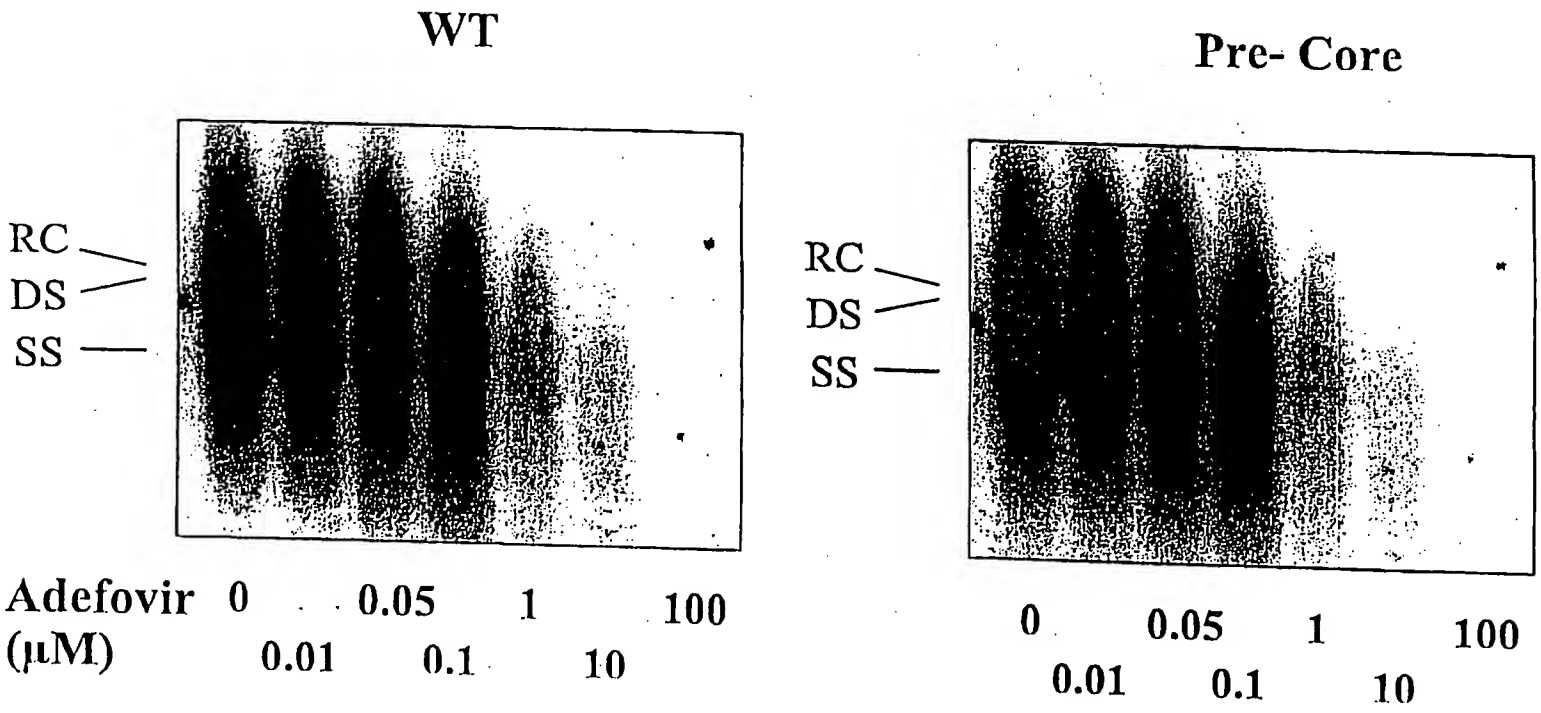

WT
Pre- Core
RC
DS
SS
RC
DS
SS
Adefovir (μM)
0
0.01
0.05
0.1
1
10
100
0
0.01
0.05
0.1
1
10
100

Figure 11A

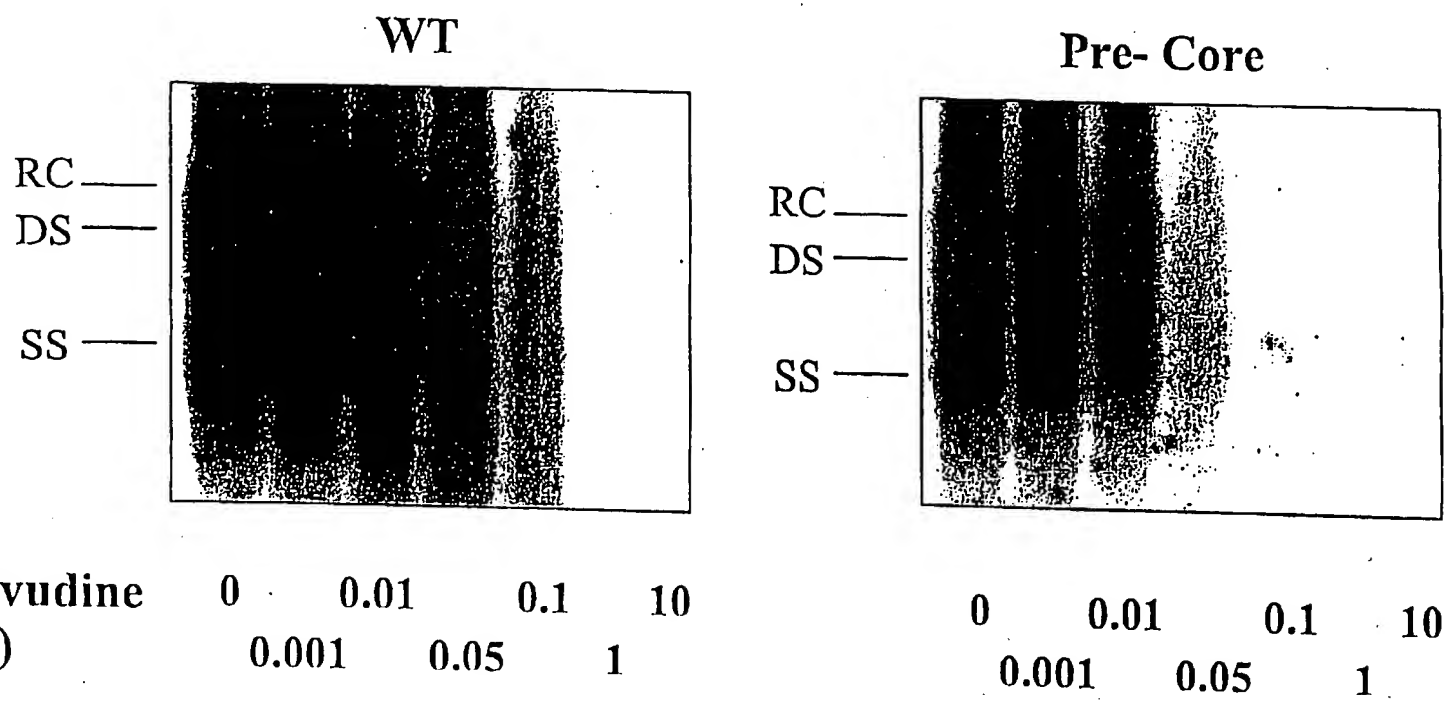

WT
Pre- Core
RC
DS
SS
RC
DS
SS
lamivudine (μM)
0
0.001
0.01
0.05
0.1
1
10
0
0.001
0.01
0.05
0.1
1
10

Figure 11B

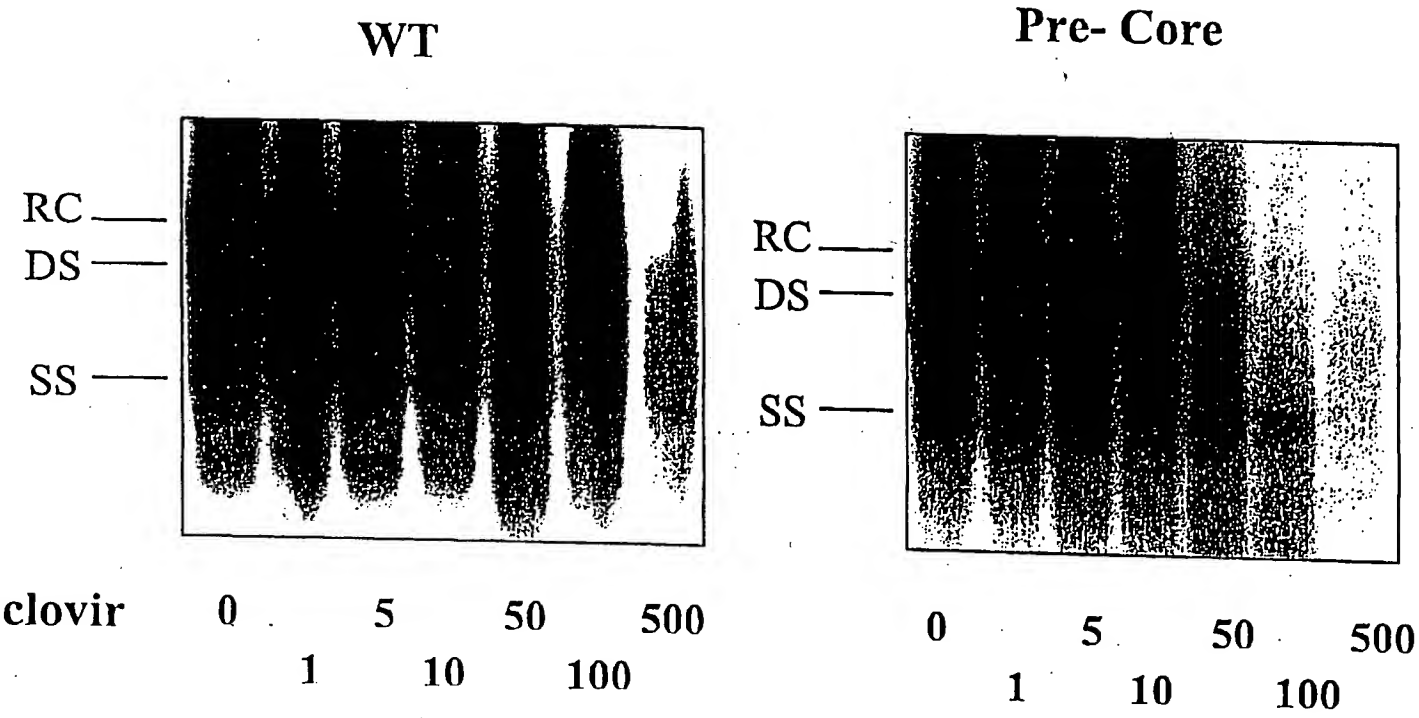
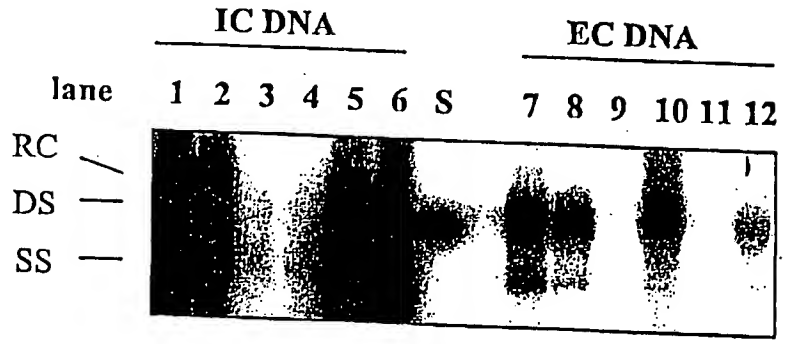

WT
Pre- Core
RC
DS
SS
RC
DS
SS
Famciclovir (μM)
0
1
5
10
50
100
500
0
1
5
10
50
100
500

Figure 11C



S	- Standard
Lane 1 & 7	- Wild type (HBV x 1.3)
Lane 2 & 8	- pre-core
Lane 3 & 9	- M550I
Lane 4 & 11	- L526M/M550V
Lane 5 & 10	- pre-core/M550I
Lane 6 & 12	- pre-core/L526M/M550V

Figure 12

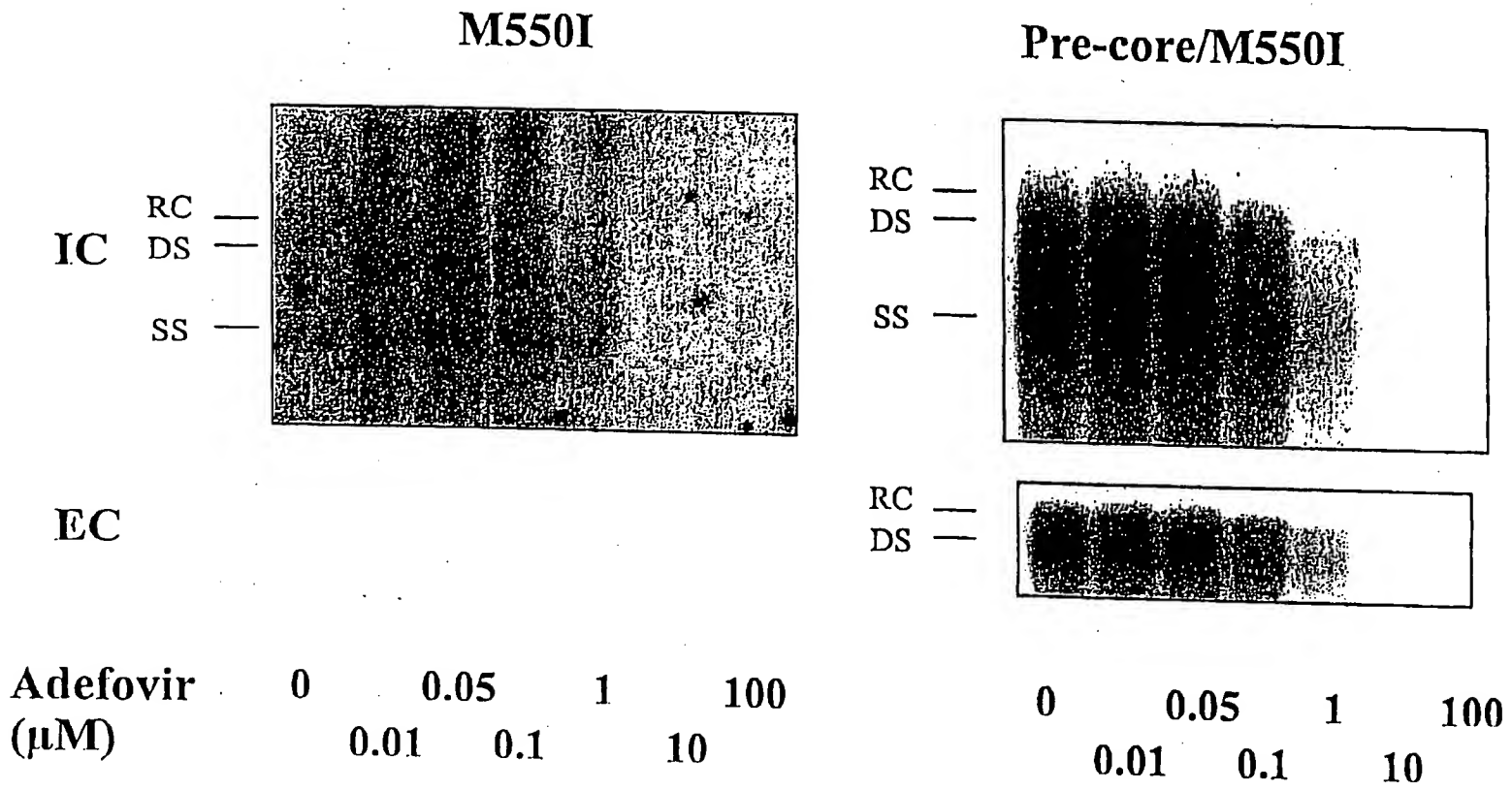

M550I
Pre-core/M550I
IC
EC
RC
DS
SS
RC
DS
SS
RC
DS
Adefovir (μM)
0
0.01
0.05
0.1
1
10
100
0
0.01
0.05
0.1
1
10
100

Figure 13A

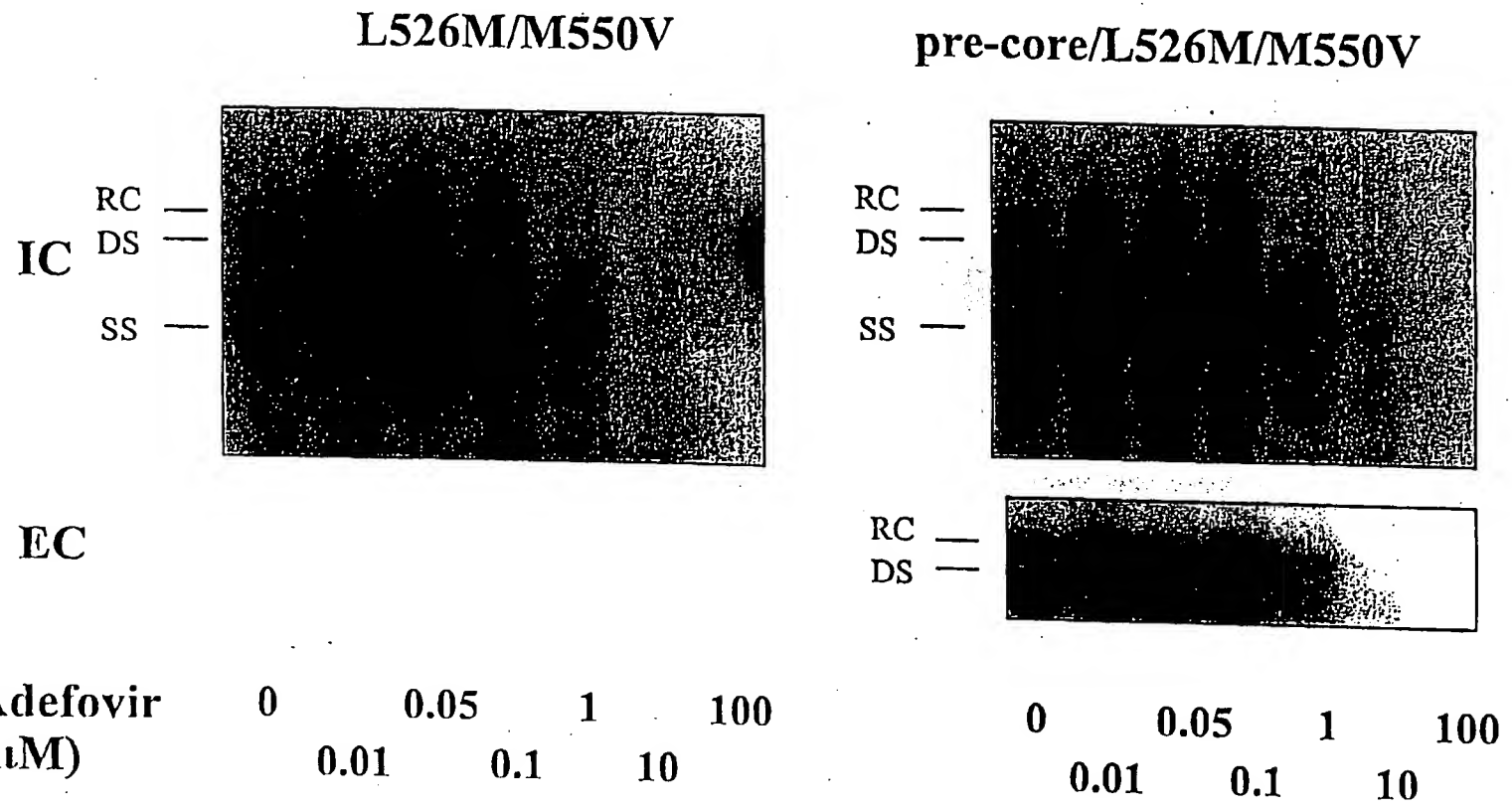

L526M/M550V
pre-core/L526M/M550V
IC
EC
RC
DS
SS
RC
DS
SS
RC
DS
Adefovir (μM)
0
0.01
0.05
0.1
1
10
100
0
0.01
0.05
0.1
1
10
100

Figure 13B

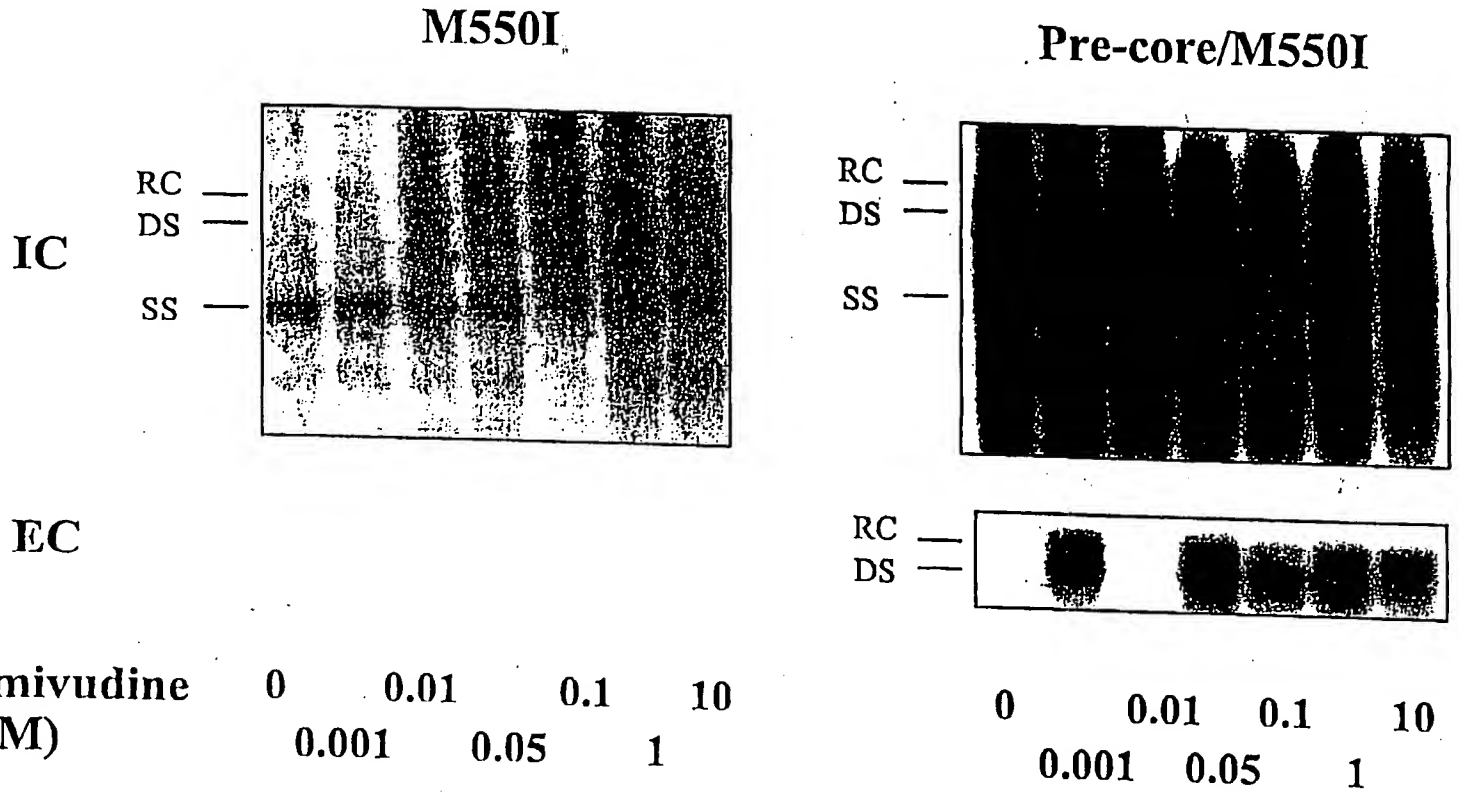

M550I
Pre-core/M550I
IC
EC
RC
DS
SS
RC
DS
SS
RC
DS
lamivudine (μM)
0
0.001
0.01
0.05
0.1
1
10
0
0.001
0.01
0.05
0.1
1
10

Figure 13C

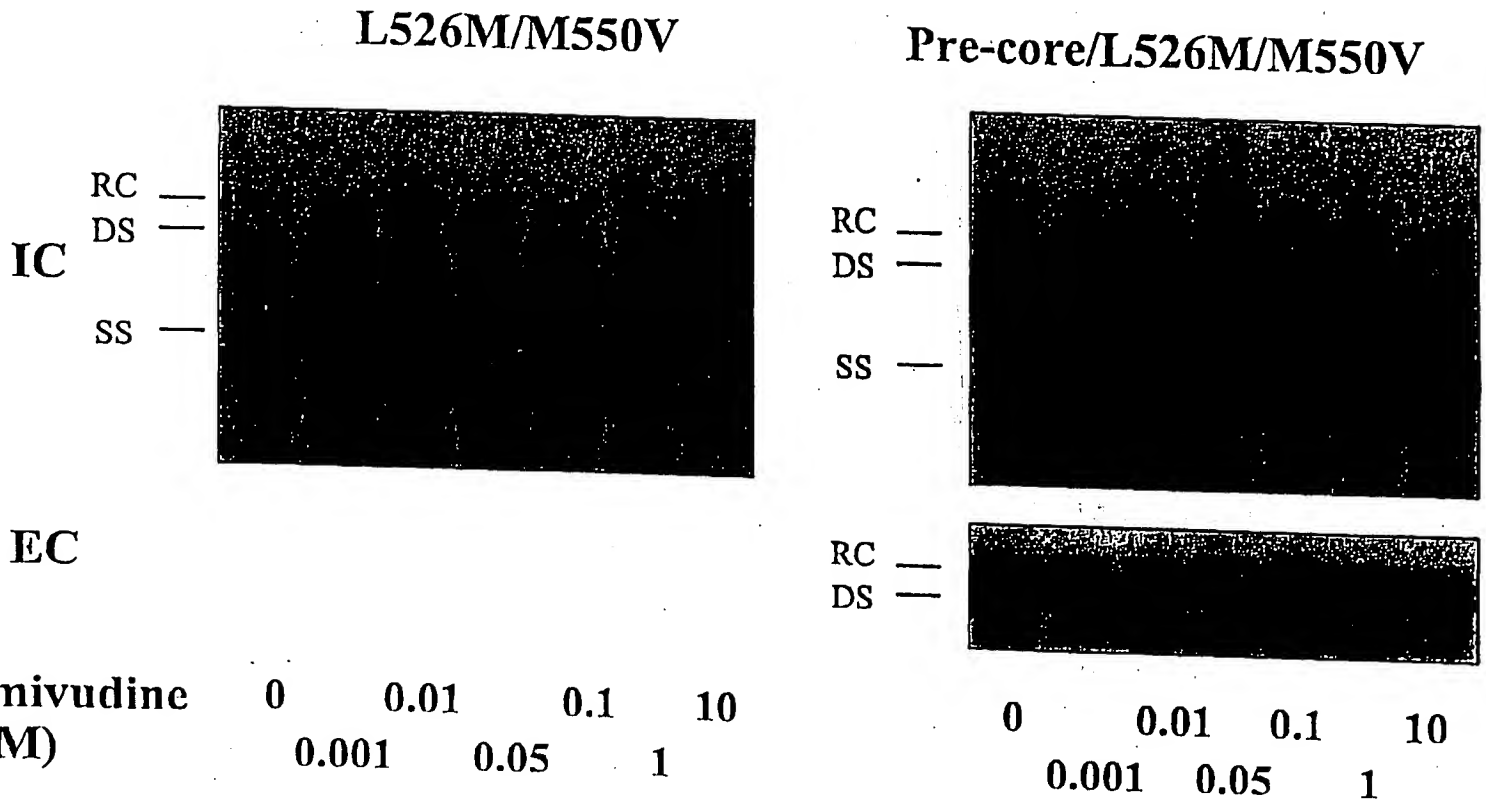

L526M/M550V
Pre-core/L526M/M550V
RC
DS
SS
IC
EC
lamivudine (μM)
0
0.001
0.01
0.05
0.1
1
10

Figure 13D

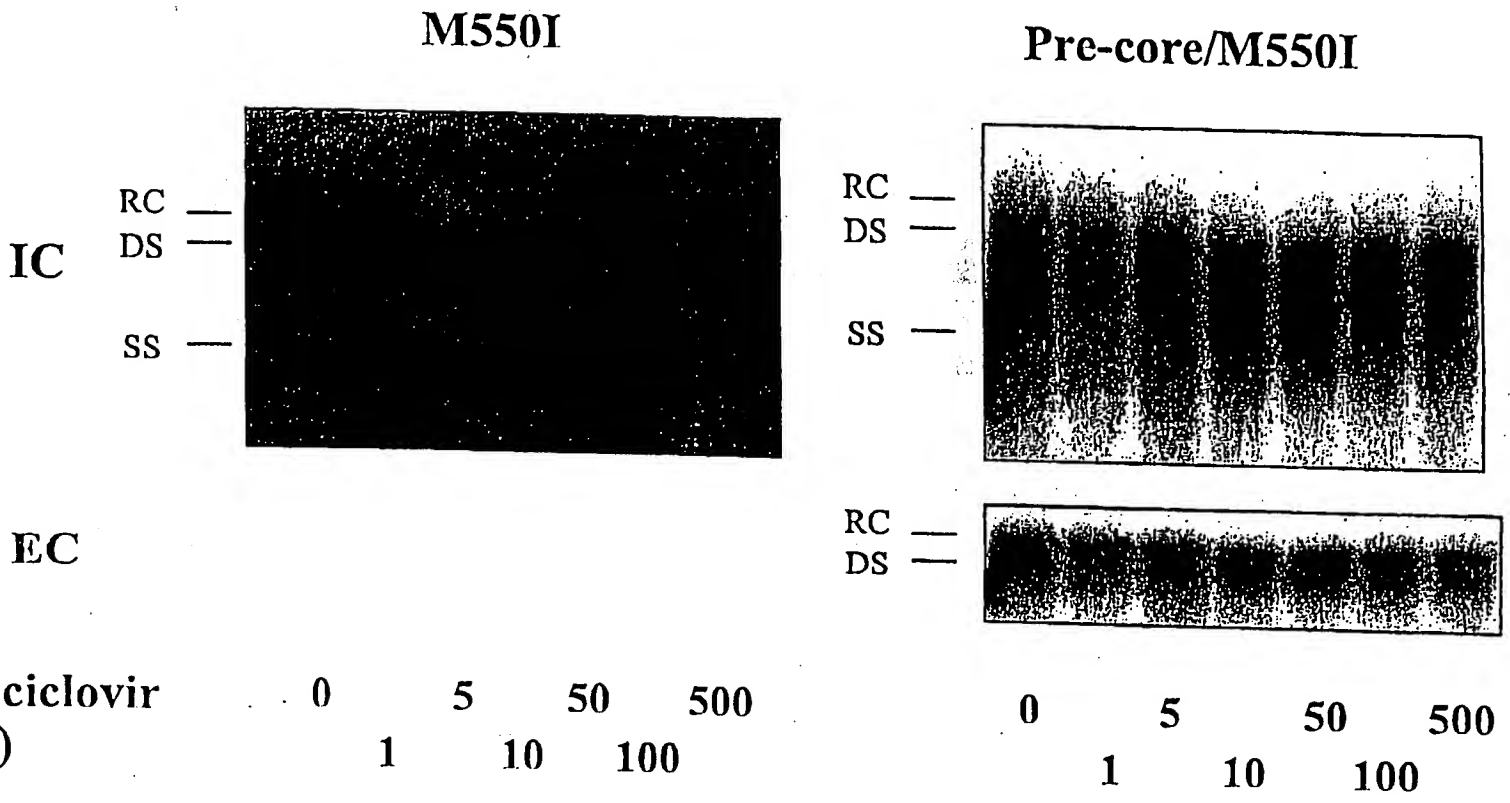

M550I
Pre-core/M550I
IC
EC
RC
DS
SS
RC
DS
SS
RC
DS
Famciclovir
(μM)
0
1
5
10
50
100
500
0
1
5
10
50
100
500

Figure 13E

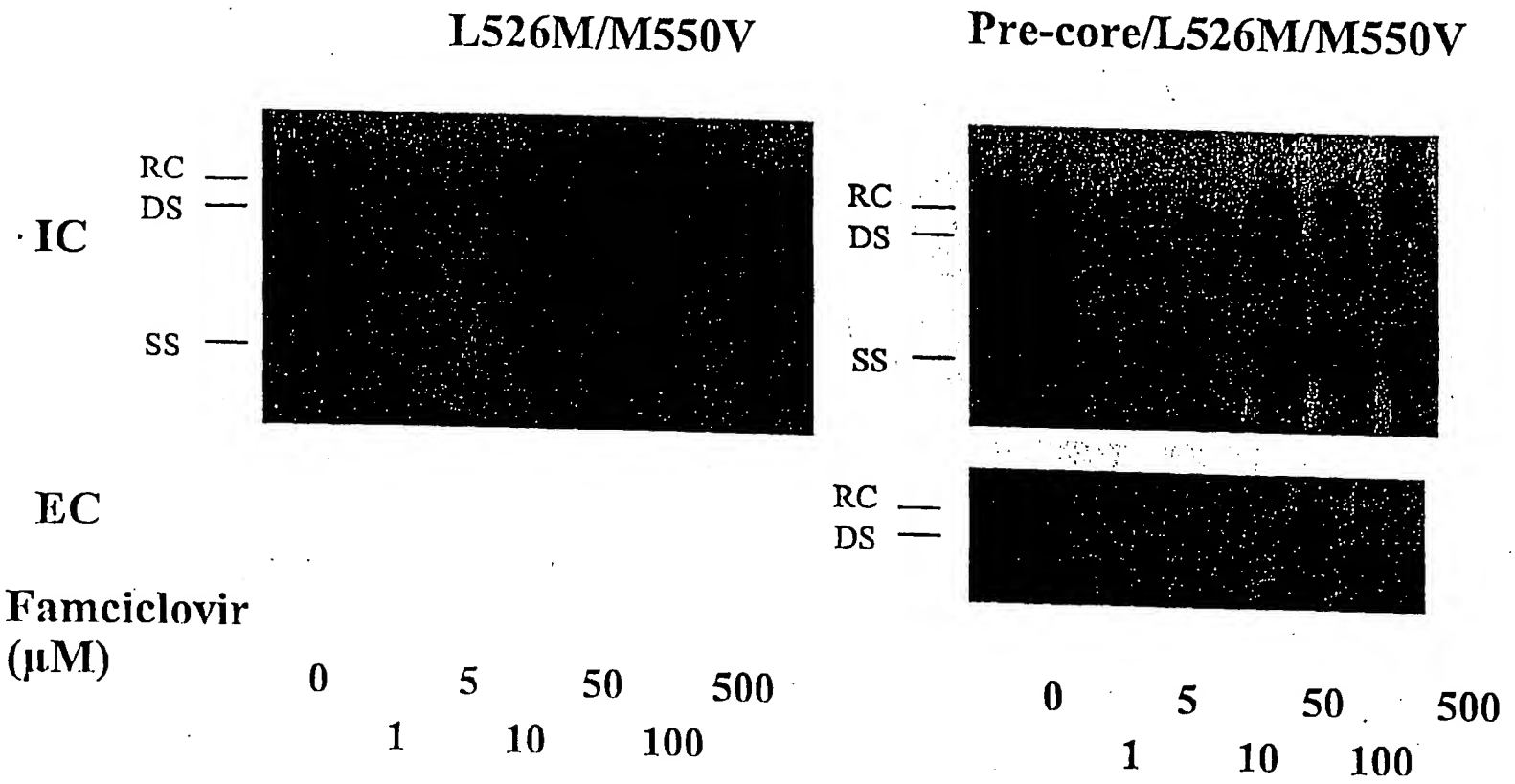

L526M/M550V
Pre-core/L526M/M550V
IC
EC
RC
DS
SS
RC
DS
SS
RC
DS
Famciclovir (μM)
0
1
5
10
50
100
500
0
1
5
10
50
100
500

Figure 13F